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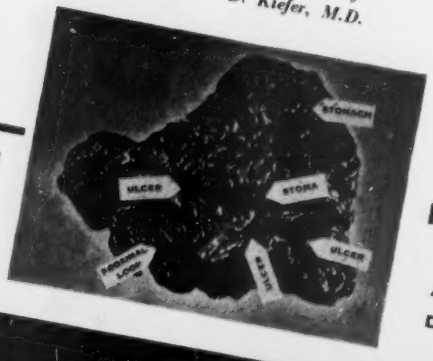

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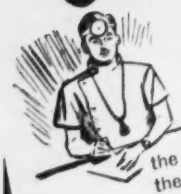

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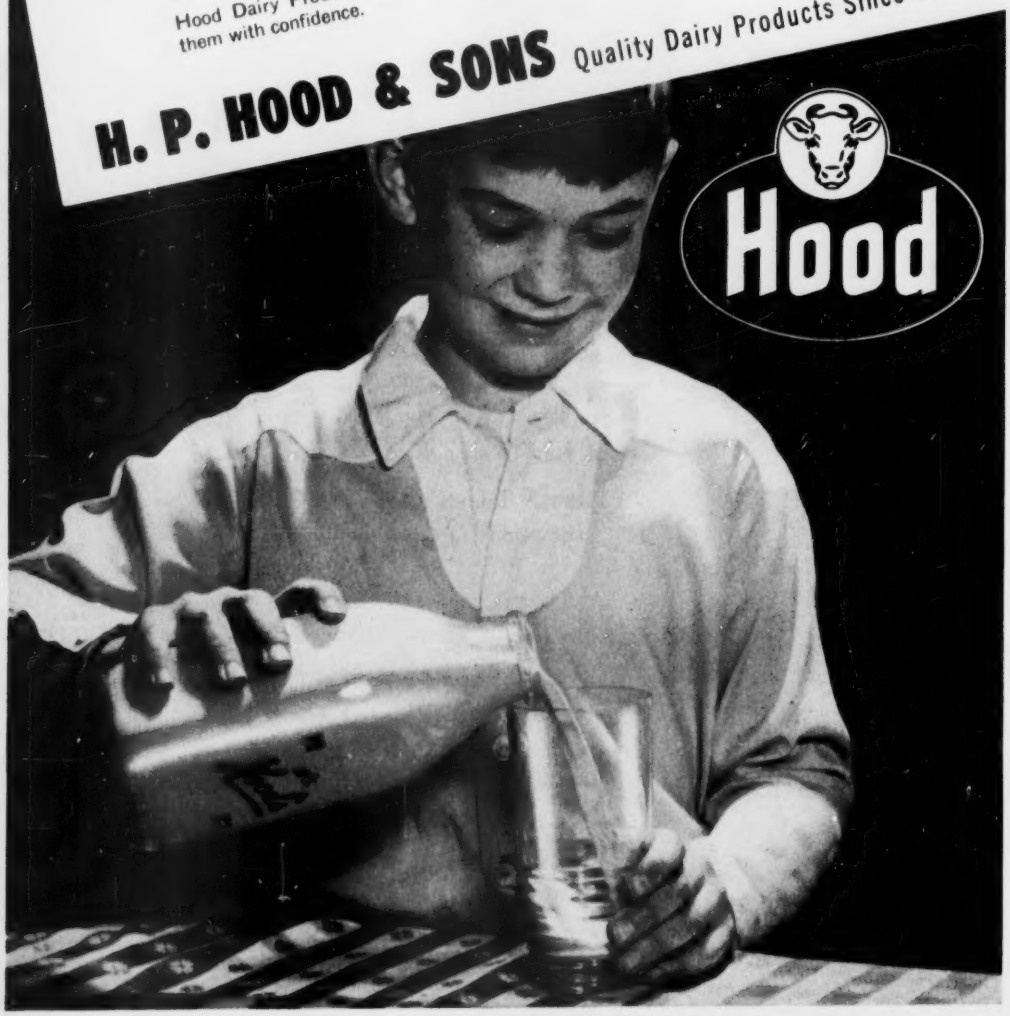

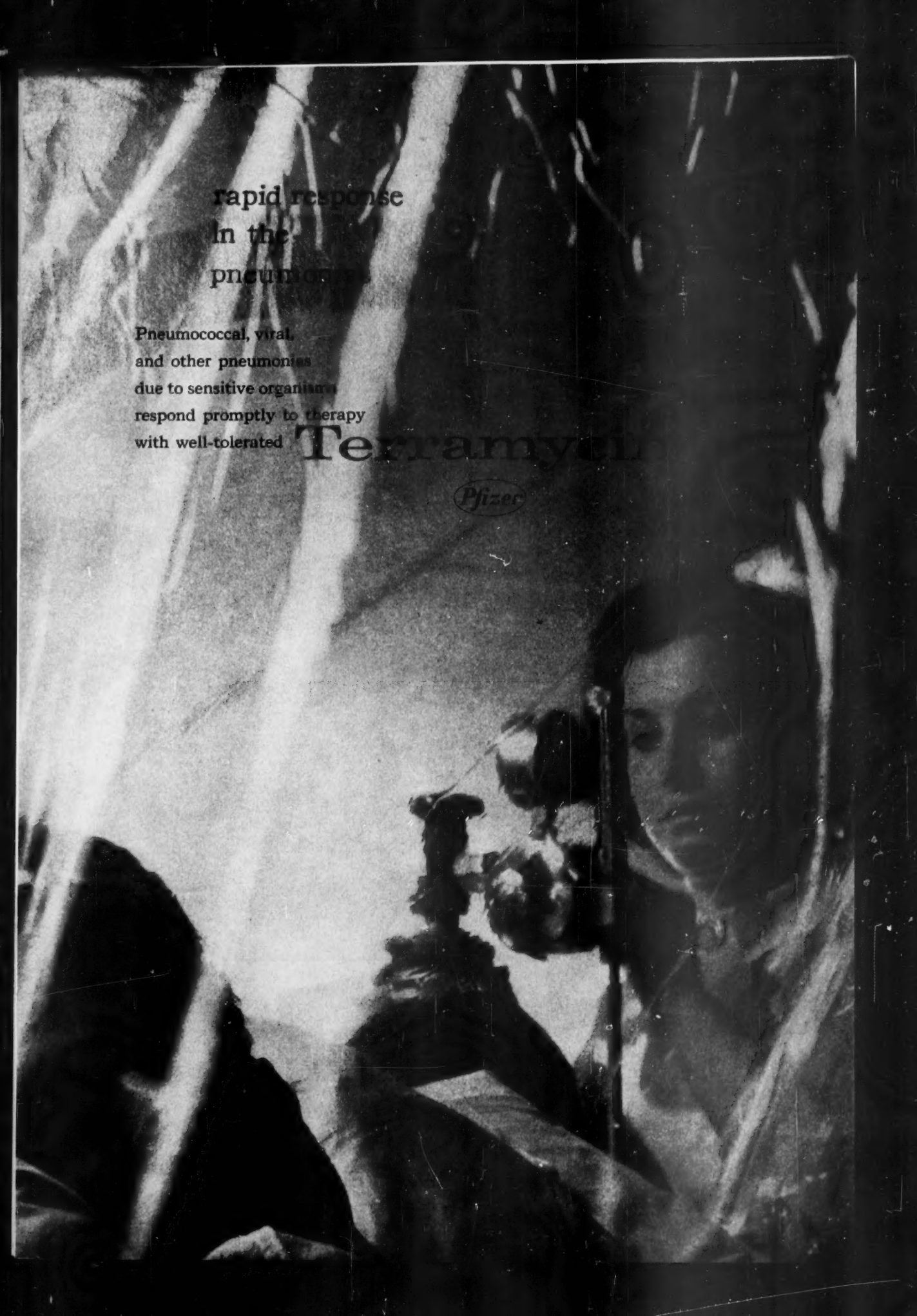
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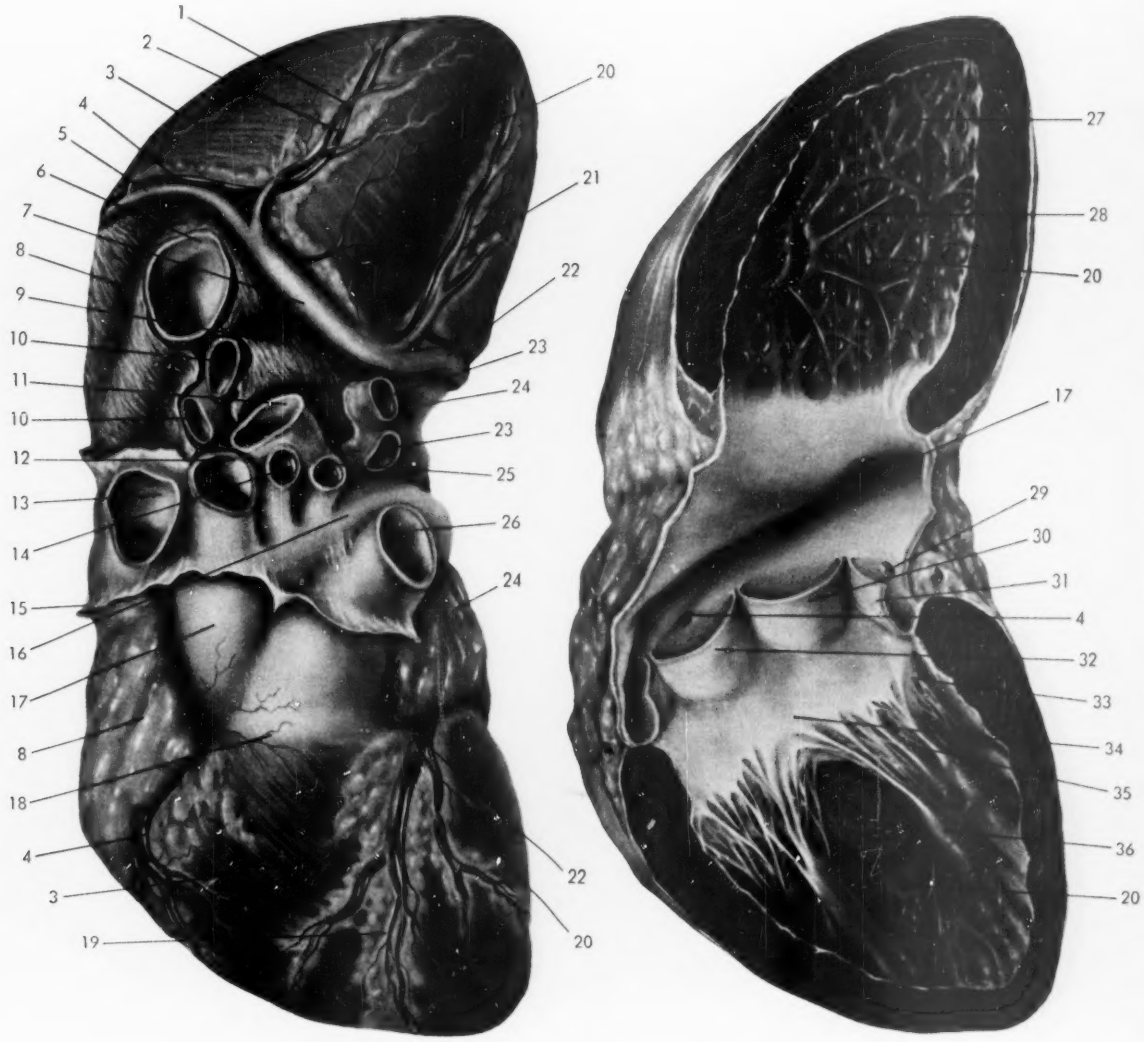

1 Middle cardiac vein
2 Posterior descending branch of right coronary artery
3 Right ventricle
4 Right coronary artery
5 Small cardiac vein
6 Inferior vena cava
7 Coronary sinus
8 Right auricle
9 Left atrium
10 Right pulmonary vein
11 Right branch of pulmonary artery
12 Innominate artery
13 Superior vena cava
14 Left common carotid artery
15 Pericardium
16 Aortic arch
17 Ascending aorta
18 Conus arteriosus
19 Anterior descending branch of left coronary artery
20 Left ventricle
21 Posterior vein of left ventricle
22 Great cardiac vein
23 Left pulmonary vein
24 Left auricle
25 Left subclavian artery
26 Left branch of pulmonary artery
27 Trabeculae carneae
28 Trabecula tendinea
29 Left coronary artery
30 Posterior semilunar valve
31 Left semilunar valve
32 Right semilunar valve
33 Posterior cusp of mitral (bicuspid) valve
34 Anterior cusp of mitral (bicuspid) valve
35 Chordae tendineae
36 Papillary muscle

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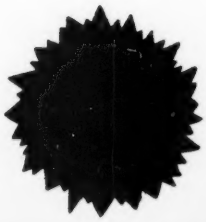

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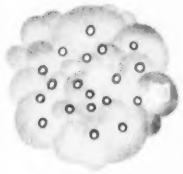

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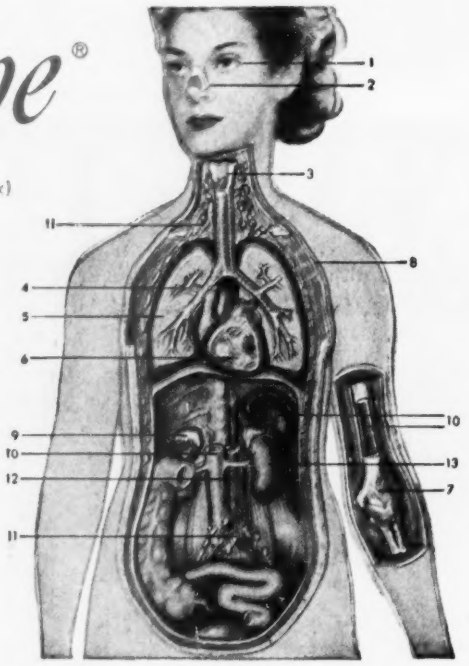

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5. Nonhemolytic streptococci	Some cases of endocarditis, genito-urinary tract infections

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THE REHABILITATION OF PATIENTS TOTALLY PARALYZED BELOW THE WAIST, WITH SPECIAL REFERENCE TO MAKING THEM AMBULATORY AND CAPABLE OF EARNING THEIR OWN LIVING*

IV. Control of Bowel Emptying

DONALD MUNRO, M.D.†

BOSTON

REHABILITATION to any practical extent is impossible for a patient with a spinal-cord or cauda-equina injury unless he can be certain that he can have infallible control of his bowel under ordinary circumstances and that, as a result, he need not fear soiling himself unexpectedly.

This desirable condition depends upon the establishment of a conditioned reflex as the result of which the large bowel empties itself only at certain prearranged times.

It is necessary to know the normal physiologic anatomy of the bowel as well as the mechanism of normal defecation to understand how such a reflex can be effectively initiated. Since the processes of digestion, absorption and elimination, in so far as the bowel is affected, are continuous and mutually interdependent, it is obvious that consideration of the part of the bowel that has to do with any one of these functions must be made in the light of the functions of the other parts. This also holds true of the anatomy and particularly of the neural anatomy. Thus, defecation is merely an end step in the process that starts in the mouth and ends in the anal canal. It is as dependent upon the proper action of the small bowel as it is upon that of the large bowel. Attempts to explain the workings of the latter without taking cognizance of the workings of the former[1] will lead to erroneous conclusions, superficial concepts and injudicious therapy.

The prime function of the whole gastrointestinal tract is to receive food (in the largest sense), prepare it for digestion, digest it, permit its absorption and then eliminate the undigested unabsorbable part. This is accomplished in successive parts of the tract from and to which the material is moved by peristalsis, which varies in rate and purpose but which is everywhere integrated by neural connections. These neural connections are made through the sympathetic and the parasympathetic systems, the activities of which are correlated by the enteric plexuses of Auerbach and Meissner. Under certain circumstances inhibition of this activity of the gastrointestinal tract may be exerted by the higher cerebral centers, but there is no evidence to support the view that initiation of bowel activity can be provided by anything except local stimuli and certainly not from the cerebral level. In general, the two ends of the tract, except for the orifices, while receiving impulses from both sympathetic and parasympathetic sources, depend chiefly for their neural impulses on the parasympathetic whereas the intervening area depends in general upon neural impulses from the sympathetic system. The enteric plexuses serve to co-ordinate these impulses in a lengthwise direction. Somatic-nervous-system connections exist only at the two orifices — the mouth and the anus. The enteric plexuses extend from the start of the nonstriated portion of the esophagus to the distal end of the rectum. The vagus or upper parasympathetic supply does not extend below the ileocecal valve,[2] while the pelvic nerves or lower parasympathetic supply are distributed chiefly to the descending colon, sigmoid and rectum. Stimulation of the vagus nerves (parasympathetic[3-5]) produces excitation, and sympathetic or splanchnic stimulation, inhibition of the activity of the intestinal musculature. Section of the vagus nerves results in a decrease, and section of the splanchnic nerves in an increase of intestinal mobility. Stimulation of the pelvic nerves (parasympathetic) causes contraction of the musculature of the descending colon, sigmoid and rectum.[2] Bronson Ray[6] has observed that total sympathectomy is accompanied by sympathetic paralysis of the small bowel ending at the ileocecal area. Kuntz[7] states that, thanks to the enteric plexuses aided by local myototic reflexes "coordinated reflex activities of the gastro-intestinal musculature may be carried out according to their normal physiologic mode in the absence of central nervous influences. . . . It seems reasonable to regard it as a reflex system capable of independent

*From the Department of Neurosurgery, Boston City Hospital.

†Assistant professor of neurosurgery, Harvard Medical School; associate professor of neurosurgery, Boston University School of Medicine; surgeon-in-chief, Department of Neurosurgery, Boston City Hospital.

coordinated reflex activity but subject to reflex motor and inhibitory influences through the central nervous system."

Control of the bowel as a step toward rehabilitation of patients paralyzed as the result of spinal-cord or cauda-equina injury has to do with the emptying function of the lower bowel or defecation. Because of its accuracy, clarity and conciseness, defecation cannot be better described than it has been by Starling[8] in the following quotation:

> "As the products of digestion pass down the colon they lose their fluid consistence, in consequence of the absorption of the water. The mass thus formed is carried down by the peristaltic contractions of the colon toward, and tends to accumulate in the sigmoid flexure. That it is not driven down at once into the rectum is due largely to the fact that the contractions which start at the ileo-cecal valve become less powerful on their way down the intestine, and do not, as a rule, affect the rectum. In healthy subjects, except just before defecation, the rectum is empty, and the presence of feces in this part of the bowel at once gives rise to discomfort, and to a desire to defecate.
>
> "When the feces have reached the rectum, their passing is still kept in check by the tonic contraction of the two sphincters of the anus, the internal sphincter composed of involuntary and the external sphincter of voluntary muscle. When the contents of the rectum are fluid or when they are forced against the sphincters by strong peristaltic contractions of the lower bowel, the action of the sphincters may be voluntarily reenforced by active contraction of the levator ani muscles, which raise and compress the lower segment of the rectum or anal canal.
>
> "Defecation is normally started by a voluntary act, although it may take place involuntarily" (as can be testified to by all those who have unintentionally passed flatus in unsuitable surroundings).
>
> "The steps of normal defecation are as follows: — The glottis being closed, a forcible expiratory contraction of the abdominal muscles takes place. The perineal muscles being relaxed at the same time, the lower part of the rectum is straightened, and a portion of the contents of the sigmoid flexure is forced down into the lower part of the rectum. The presence of a foreign body in this part of the rectum irritates the mucous membrane and excites reflexly the rest of the act. Strong peristaltic contractions take place along the whole of the descending colon, sigmoid flexure, and rectum, while both sphincters are relaxed thus forcing out the contents of the bowel. The last section of the rectum at the close of the act is emptied by a forcible contraction of the levator ani and other perineal muscles."

The detailed process by which this emptying of the rectum is accomplished is quite analogous to the emptying of the bladder and the activity of its outlet. This is to be expected because the segmental nervous control is the same for both organs and lies in the second, third and fourth sacral segments of the spinal cord. As noted above, the reservoir or storage space for the fecal mass is in the sigmoid and descending colon. From here the material is moved to the rectum, in which, acting as a foreign body, it serves as the sensory stimulus of a reflex, the motor portion of which causes a contraction of the rectal wall and simultaneous relaxation of the internal anal sphincter. This permits entry of fecal material into the upper end of the anal canal, the lower end of which is normally kept closed by a contracted external sphincter. This invasion, acting as a sensory stimulus, in its turn sets up a second reflex, the motor component of which causes relaxation of the external sphincter and, if they are still contracted, the relaxation of the muscles of the perineum, thus permitting the final expulsion of the rectal contents. During this process, unless inhibited by impulses from the suprasegmental parts of the central nervous system, peristalsis continues to move the contents of the reservoir (the sigmoid and descending colon) into the rectum for further emptying, their place being taken by the orderly processing of further material from the small and rest of the large bowel. Inhibition of emptying may also be accomplished by voluntary closure of the anal canal through contraction of the external sphincter. This muscle, being supplied by the somatic nervous system, is under voluntary control and can be contracted and relaxed at will. It is apparent that except for the occasional individual action of this last structure, the action is everywhere dependent upon integrated activity of the whole tract and that the removal of one link in the anatomicophysiologic chain will be sufficient to disrupt the whole process. Thus, excision of the rectum will necessarily denervate the internal sphincter, and the best sphincter action that can be expected even in the face of an intact canal and pudic nerve supply is that provided voluntarily by the victim through his external sphincter. With the additional denervation — intentional or otherwise — of the latter structure sphincteric control will be impossible regardless of the preservation of the anal canal and whether or not anastomosis is made between it and the sigmoid or descending colon. Excision of the colon or sigmoid above the level of the rectum followed by an appropriate anastomosis and the maintenance of the neural connections to the latter organ assures — other things being equal — orderly, controlled evacuation of the contents but no capacity for storage, thus forcing the sphincteric mechanism to hold back contents more fluid than they should be, with resultant mechanical leakage from time to time. It is not known whether the cut enteric plexus will unite again in the bowel wall, even after an end-to-end anastomosis, when a section of it has been removed. If it will not, orderly longitudinal peristalsis appears to be impossible. Thus, the large bowel proximal to a colostomy might be expected to dilate gradually when subjected to overloading if for no other reason than that the peristaltic stream has been brought to an end with the colostomy. It is well known that this condition does develop, and Swenson[9] has recently also emphasized that anatomic division of the bowel is not a prerequisite for such dilatation (even in excessive amounts) and that physiologic division by local spasm can accomplish the same thing. It may be possible after the lapse of sufficient time to get information about the neural union of cut enteric plexuses from a late study of his cases of Hirschsprung's disease.

Material

The anatomicophysiology briefly outlined above has been practically entirely the result of observation made on experimental animals. My experience with men and women who have suffered various degrees of segmental nervous-system injury has confirmed these conclusions from a clinical point of view as applied to human beings. The material is all from the neurosurgical department at the Boston City Hospital and comprises only civilian patients. Seventeen suffered from epidural spinal abscess, 2 from multiple sclerosis, 2 from a spinal-cord tumor and 289 from injury, there being a total of 310 patients. One hundred and sixty-one of these suffered from lesions in the cervical, 76 in the thoracolumbar and 30 in the lumbosacral cord. Forty-two had cauda-equina lesions, and 1, a patient with multiple sclerosis, had generalized spinal-cord involvement.

The cord injuries that were most likely to produce abnormal bowel reactions as observed at the time of the patient's admission to the hospital were those of the lumbosacral cord, with those of the thoracolumbar cord next (Table 1). This could have been predicted in view of our knowledge of neural connections between these regions and the bowel. An abnormal reaction was considered to be present if the abdomen was distended, tense, spastic or rigid to palpation and without peristalsis; or if the patient was continuously vomiting or was incontinent of feces or had diarrhea. Spinal shock was also a factor and was probably of more importance than the part of the cord that was injured. The types of pathology that were most likely to produce abnormality of the bowel at the time of hospital admission were a transection and the compressive lesions (Table 2). Thus, it is apparent that the function of the entire gastrointestinal tract can, but need not, be affected and its activity rendered abnormal by any type of injury to any part of the spinal cord and cauda equina. Undoubtedly, as noted above, the effect of spinal shock, however (by its influence on all reflex activity), plays as much or more of a role in the production of gastrointestinal areflexia and paralysis than either the level or type of cord injury.

Table 1. *Bowel Reactions at Admission — Effect of Level of Injury.*

Level	Total Cases	Abnormal Reaction	Percentage
Cervical	148	43	29
Thoracolumbar	74	26	35
Lumbosacral	30	13	43
Cauda equina	40	10	25
All levels	293	91	31
No note	17	—	—

The condition of the bowel both at admission and at discharge was known in 289 patients (Table 3). It could be classed as either normal or abnormal at admission and as normal, abnormal or controlled at discharge. Of these, 197 were normal at admission — 132, or 67 per cent, being also normal at discharge. The death rate in this group (31 having normal and 11 having abnormal function at the time of death) was 25 per cent. Ninety-two, or 32 per cent, had abnormal bowel function at admission — 34 (37 per cent) being normal at discharge and 33 (36 per cent) being abnormal at both admission and discharge. The death rate in this group (14 having normal and 20 having abnormal function at the time of death) was 45 per cent. It appears from this experience that the condition of the bowel at the time of admission to the hospital (and particularly if the patient is admitted at once after the accident) is of some prognostic value in that the subsequent mortality is 20 per cent higher if the activity of the bowel is abnormal at that time.

Table 2. *Effect of Pathology on Bowel Reactions at Admission.*

Pathology	Total Cases	Abnormal Reaction	Percentage
Transection	22	8	36
Contusion	22	6	27
Edema	4	1	25
Hemorrhage	45	13	29
Total without compression	93	28	30
Compression alone	76	24	32
Compression with any of above	99	37	37
Total with compression	175	61	35
Miscellaneous pathology	25	4	16
No note of pathology	17	—	—
Grand totals	310	93	30

Table 3. *Bowel Condition at Discharge.*

Condition at Admission	Condition at Discharge	Living Patients	Dead Patients	Totals
Normal (197 cases)	Normal	101	31	132
	Abnormal	17	11	28
	Controlled	25	0	25
	No note	5	7	12
	Totals	148	49	197
Abnormal (92 cases)	Normal	20	14	34
	Abnormal	13	20	33
	Controlled	14	0	14
	No note	4	7	11
	Totals	51	41	92
Normal and abnormal	Normal	121	45	166
	Abnormal	30	31	61
	Controlled	39	0	39
	No note	9	14	23
	Totals	199	90	289
No note or no pathology (21 cases)	No note	8	9	17
	No pathology	4	0	4
	Totals	12	9	21
Grand totals		211	99	310

One hundred and sixty-six, or 57 per cent, had normal bowel action at discharge. Thirty-nine patients, or 14 per cent, who had normal bowel activity on admission that subsequently became abnormal during their stay, or had abnormal activity throughout their stay, were discharged with controlled bowel activity. There were no deaths in this category. This last group includes those with transected spinal cords, damage to the lumbosacral cord and injuries of major import to the cauda equina. These are the patients that are most in need of therapy if bowel control and freedom from the fear of unexpected soiling are to be provided. It is also into this group that the patients fall who have sustained such an injury as to force the bowel difference between life and death. Bladder distention is controlled by tidal drainage. In the cervical injuries the chest is strapped tightly while in inspiration with wide adhesive plaster as described elsewhere[10] and oxygen administered through a nasal catheter at the rate of 2 liters per minute. These procedures, together with traction immobilization, have proved life saving, particularly in these and the upper-thoracic-cord injuries. When peristalsis is again audible and there is no further dilatation of the stomach, fluids, followed by gruel in small amounts (60 to 120 cc.) at frequent intervals (every one or two hours), are started. This diet is increased gradually until the patient is taking by mouth a mixed diet containing 3000 calories and

TABLE 4. *Distribution According to Pathology of Patients with Bowel Activity at Discharge.*

Bowel Condition on Admission	Level of Injury	Contusion Alone	Transection Alone	Compression with Transection	Compression with Contusion	Compression Alone	Atrophy	Post-Spinal Anesthetic	Totals
Normal	Thoracolumbar	0	1	13	0	0	0	0	14
	Lumbosacral	1	1	0	0	5	0	0	7
	Cauda equina	1	0	0	0	2	0	1	4
	Totals	2	2	13	0	7	0	1	25
Abnormal ..	Thoracolumbar	0	0	2	0	2	0	0	4
	Lumbosacral	0	0	2	2	3	1	0	8
	Cauda equina	0	0	0	0	2	0	0	2
	Totals	0	0	4	2	7	1	0	14
Grand totals		2	2	17	2	14	1	1	39

to act on a pure segmental reflex (transected cords) or on a partially denervated basis (lumbosacral-cord and cauda-equina injuries). These 39 patients are, therefore, the ones in whom the institution of a conditioned reflex, under the name of bowel training, has been particularly effective. No patients with a cervical-cord injury fall into this class. The distribution of these 39 patients in accordance with level of cord injury, pathology and normality of bowel action at admission is shown in Table 4. It is to be noted that 20 of the 39 patients had transected cords, the one atrophic cord being a physiologic transection.

Treatment

Acute Stage

While spinal shock is present and the abdomen remains silent the patient is given no food or fluids, including water, by mouth. A rectal tube is inserted and left in place for one out of every two hours. If there is vomiting, Wangensteen suction is instituted. Care must be taken also to keep the stomach empty of swallowed air. This is a particularly common complication in the cervical cases. If the dilated stomach is not promptly decompressed by intubation, the consequent interference with affective action of the diaphragm may make the 150 gm. of protein per twenty-four hours unless peristalsis again stops. No drugs, applications to the abdomen and particularly no laparotomy should be given, applied or performed during the period of intestinal paralysis. If this therapy is instituted at once after the accident and particularly if it is rigorously enforced, especially the ban on ingestion of water, distention will not develop.

Intermittent Stage

With the return to a normal diet and for as long a period as the bladder remains atonic or hypertonic or is not reflex in its activity as determined by repeated cystometrograms, the bowels are controlled by soapsuds, oil-retention or milk and molasses enemas supplemented by manual extraction of any fecal impactions. With the evidence, as provided by the demonstration of a reflex bladder, that segmental reinervation of the bowel is again established, institution of bowel training can be started. As soon as the patient can be sufficiently mobilized to use a commode or the toilet, the use of a bedpan should be abandoned. Bowel training cannot be accomplished and should not be started while there are uncontrolled involuntary spasms such as the so-called "mass reflex," or while spinal shock and hence any such complication as a major infection,

inanition, exhaustion and hypoproteinemia and the like are present. All necessary steps should be taken at this time to correct such conditions by operation or other appropriate therapy.

The final and most important precedent to bowel training is that the anal reflex must be active. This means that the external anal sphincter is properly innervated and, by implication, since they arise from the same sacral segments, that the nerve supply of the large bowel from the sigmoid flexure through the internal rectal sphincter is also intact. The contrary is equally true and evidence of flaccidity of the external sphincter and its consequent denervation may mean changes that will make it impossible to accomplish bowel training.

Bowel Training

This depends upon the establishment of a conditioned spinal bowel reflex. Except that it is easier to fulfill in the absence of intact suprasegmental connections, this requirement is the same as that necessary for proper bowel evacuation in normal adults. It is well recognized that in the absence of disease of the bowel and in an otherwise normal person, normal regular defecation can only be accomplished by having the patient go to stool at the same time every day or every two days; by eliminating psychologic inhibitory impulses coming from the higher central-nervous-system levels by having the toilet clean, the seat comfortable, the room warm and adequate time available, and by the elimination of as much as possible of the intentional or voluntary effort that is otherwise made by the individual. These various criteria, if they are met, permit the bowel, in a normal adult, to function on a purely reflex basis exactly as it did during early childhood, the only difference being that the adult inhibits the movement of the fecal mass from the colon and sigmoid into the rectum until a certain time of day and condition of surroundings have been met.

Any patient with an injury of the spinal cord or cauda equina who has had the problem explained to him and who understands the criteria that must be met can learn bowel training even in the presence of paralysis of the trunk and legs. As the first step in conditioning the necessary reflexes a soapsuds enema is self-administered by the patient every morning at some previously chosen time, which will thereafter be unalterable. The enema should be as small as is compatible with ensuring emptying of the bowel. The patient does best if he is seated on the toilet for the procedure, next best if he is on a commode and least well on a bedpan. Efforts should be made, therefore, to mobilize him sufficiently to make it possible for him to use a toilet. Moreover since a maximum of general activity is also helpful for the purpose at hand he should be taking bed and mat exercises and, if possible, ambulation training as well at this time. The last is not essential, however. After a week of this bowel routine the enema should be omitted every third day and a dose of milk of magnesia, by mouth, should be substituted for it. The size of the dose and time of administration of the milk of magnesia will have to be determined by experiment. The dose should be just large enough to ensure a bowel movement. The time at which it is administered must be such as to effect evacuation at the time at which it has already been predetermined that the bowel is to move. After this routine has been established the remaining enemas are gradually eliminated one by one, milk of magnesia by mouth being substituted for each, until the patient no longer is being given any enemas and his bowel is stimulated only by the milk of magnesia. Thus, reflex emptying of the bowel has been conditioned first as to time between evacuations, secondly as to stimulation of the rectum locally by the enemas and thirdly as to stimulation of large-bowel peristalsis generally by the milk of magnesia. In order that the fecal mass may be maintained in the proper soft-solid consistence and the inside of the intestinal tract kept well greased, mineral oil is given in addition throughout this period. It should be started as 30 to 60 cc. (1 or 2 ounces) given by mouth night and morning, and kept at this level until it leaks from the rectum. Thereafter the dose should be gradually diminished until there is no longer any leakage and then maintained at that level until the bowel training is completed.

The final step in bowel training is to eliminate the milk of magnesia. This is done by gradual, regular, periodic withdrawal. This final step eliminates all conditioning stimuli except the temporal one. If the patient will continue to go to stool every day or every other day at the time he has already chosen and conditioned his bowel to move at, he can be sure that, barring intestinal upsets or disease, his bowel will empty itself at the designated time and at no other time. The knowledge that he will not unexpectedly soil himself because of this ability is an essential prerequisite to mobilization, ambulation and rehabilitation. Fortunately, this is a relatively easy skill to acquire.

Results

Bowel training as described has been carried out on 42 of the 310 patients in this series. Where it has been successful the patients who acquired this skill have been free of accidental soiling for periods varying from one to seven years. There can be no doubt that a conditioned reflex that will permanently regulate bowel discharge can be established in the absence of all somatic neural connections between the brain and the spinal cord and without the need for enemas, suppositories, catharsis or digital stimulation.

Of the 310 patients in this series 106 died in the hospital and cannot be considered in relation to the

success or failure of bowel training. Because of insanity (2 cases), treatment prior to the adoption of the method (3 cases) and sudden death during training (2 cases) 7 others must be eliminated as well. This leaves 197 patients that were potential candidates for this therapy. One hundred and twenty-three, or 62 per cent, recovered control by themselves without added training. Fourteen, or 7 per cent, were unco-operative and refused to be trained even though they were suitable for and needed the training. In 12, or 6 per cent, the end result of the training was unknown for various reasons, and in 3, or 1.5 per cent, the symptoms at the last analysis were traceable to functional abnormalities rather than organic disease. In 3 cases, or 1.5 per cent, the method failed for some undeterminable reason.

Thus, 74, or 36 per cent, of 204 patients with injuries of the spinal cord and cauda equina should have been discharged with bowel control as the result of bowel training. This desirable result was unobtainable in all cases because 14, or 18 per cent, of the patients would not co-operate; in 9, or 12 per cent, the pathology indicated the need for its use but unfortunately there is no note of its success or failure, and in 3, or 4 per cent, the pathology was such that bowel control might have been needed but again no note is available about the outcome.

The method failed in 3 patients, or 4 per cent, for some unknown reason, although properly used with the enthusiastic co-operation of the patients. This can only be ascribed to unrecognized inherent deficiencies.

The method succeeded in 42 of the 74 cases in which it was needed — in 39 during the hospital stay and in 3 after discharge. This is 57 per cent and is a figure that undoubtedly errs on the side of conservatism.

Summary

A method of obtaining virtually infallible control of bowel emptying in the presence of spinal-cord and cauda-equina injuries of major import is presented. It is based on the initiation and maintenance of a conditioned reflex. The neurophysiologic and practical aspects of the control of bowel emptying in the normal person are reviewed. A detailed report of the response of the bowel to acute spinal-cord and cauda-equina injuries in 310 patients and the methods devised for the treatment of this as well as the more chronic manifestations is described under the term "bowel training."

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THE USE OF *RAUWOLFIA SERPENTINA* IN HYPERTENSIVE PATIENTS*

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BOSTON

Rauwolfia serpentina (*Ophioxylon serpentinum*) has been used in India for many years to treat a variety of diseases that at first thought appear to bear little similarity to one another. These include insanity, epilepsy, insomnia, hysteria, eclampsia and hypertension. On reflection, however, these various diseases could have a common denominator if they were all relieved symptomatically by a sedative or a "relaxing" drug such as *Rauwolfia*. Our attention was drawn to the drug because reports of its hypotensive effects seemed to be fairly well documented; indeed, the conservative claims made for it by several authors increased rather than diminished our interest in its possible use for the treatment of hypertension.

Bhatia,[1] in 1942, briefly reviewed the reported pharmacology of the drug and observed its clinical effects in patients with "essential" and with "renal" hypertension. He stated that the drug in the form of Serpina tablets (½ to 1 tablet at bedtime) was well tolerated and caused a moderate lowering of blood pressure:

> [It was] particularly useful in relieving the nervous symptoms of high blood pressure, such as headache, tinnitus, vertigo, giddiness, insomnia, etc. Every patient remarked that he got very good sleep with this drug. In

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all probability, the beneficial effect of the drug in high blood pressure is produced through its action on the nervous system.

Bhatia did not comment on the bradycrotic effect of the drug.

In 1943, Gupta, Deb and Kahali,[2] in a paper on the use of the drug in the treatment of mental disorders, stressed its sedative effect and noted in a patient with epilepsy that the blood pressure decreased to 80 systolic, 56 diastolic, and the pulse to 54, "necessitating withdrawal of the drug for 2 days." Roy,[3] in 1950, also noted that the drug in manic patients slowed the pulse rate markedly.

In 1949 Vakil[4] presented a paper entitled "A Clinical Trial of *Rauwolfia Serpentina* in Essential Hypertension." He mentioned a ten-year personal experience, and remarked on the vote by 46 of 50 Indian physicians whom he polled by mail as being in favor of this drug over all others for the treatment of hypertension. In an experimental trial of the drug alternating with placebo control, he found that 44 per cent of patients showed lowering of blood pressure by 20 or more systolic and by 10 or more diastolic. Chakravarty, Rai Chaudhuri and Chaudhuri,[5] in 1951, noted in 15 cases an average decrease of 18.5 systolic and 16.4 diastolic on the tenth day of treatment. Thus, it appears from the literature that *Rauwolfia serpentina* is a hypotensive drug of moderate potency, that it has a sedative effect that may be related to the symptomatic relief that patients describe, and that it slows the pulse rate.

The purpose of this paper is to summarize our experience with this drug, which when given alone has duplicated essentially the results reported by others, and when given in conjunction with other hypotensive agents, notably hydrazinophthalazine, or *Veratrum viride*, has appeared to exert a remarkable additive, if not synergistic, hypotensive effect.

TABLE 1. *Effects of Serpina Alone in 15 Patients.*

PATIENT	AGE	SEX	CONTROL OBSERVATION			OBSERVATION UNDER TREATMENT		
			DURATION OF OBSERVATION	BLOOD PRESSURE	PULSE	DURATION OF THERAPY	BLOOD PRESSURE	PULSE
	yr.		*wk.*		*beats/min.*	*wk.*		*beats/min.*
C. C.	51	F	4	220/125	70	20	180/105	60
F. D.	43	F	12	175/115	88	12	140/90	65
K. Z.	52	F	6	230/130	88	24	205/120	78
L. F.	56	F	4	230/120	88	16	215/95	65
T. N.	53	F	3	260/130	67	24	225/115	64
E. C.	62	F	8	190/100	97	20	190/95	76
W. W.	28	M	100	140/100	84	16	115/80	70
L. F.	52	M	2	180/110	85	24	160/90	70
O. B.	44	M	1	160/110	88	13	125/80	72
H. F.	43	F	4	160/90	100	60	120/70	84
R. P.	40	F	8	160/100	84	16	125/75	76
S. B.	39	M	1	210/130	84	24	120/75	64
W. F.	58	M	100	175/95	76	18	150/90	64
E. R.	54	M	2	160/90	80	30	120/80	76
E. C.	57	F	3	190/120	91	3	160/100	80

TABLE 2. *Effects of Serpina and Veratrum Viride in 9 Additional Patients.*

PATIENT	AGE	SEX	CONTROL OBSERVATION			OBSERVATION ON SERPINA THERAPY			OBSERVATION ON SERPINA AND VERATRUM VIRIDE THERAPY		
			DURATION OF OBSERVATION	BLOOD PRESSURE	PULSE	DURATION OF THERAPY	BLOOD PRESSURE	PULSE	DURATION OF THERAPY	BLOOD PRESSURE	PULSE
	yr.		*wk.*		*beats/min.*	*wk.*		*beats/min.*	*wk.*		*beats/min.*
N. F.	40	M	156	160/120	68	8	140 80	65	4	140/95	72
A. B.	48	F	3	195/100	70	16	190/100	73	2	170/95	88
E. F.	63	F	4	210/120	104	—	—	—	20	200/110	90
M. S.	44	F	16	185/115	80	20	150/95	63	10	160/95	68
M. H.	54	F	5	170/110	72	8	150/95	63	2	145/90	60
F. H.	62	F	12	220/115	95	12	150/90	80	16	155/90	75
E. A.	41	F	10	160/110	120	—	—	—	40	120/80	80
A. C	31	M	4	225/145	110	7	175/105	80	20	125/80	84
I. B.	45	F	2	190/125	100	2	190/115	78	8	150/100	72

Material and Methods

The subjects were unselected clinic or office patients with hypertension that was usually diagnosed as "essential," but in a few cases as "renal." Most of these patients had had the routine clinical and laboratory studies used in this hospital to evaluate the hypertensive state, including complete history, physical examination, urinalysis and fractional phenolsulfonephthalein test, electrocardiogram and cardiac fluoroscopy, sedation test and cold and posture test. After at least several weeks of observation, either on no medical treatment or on treatment with some other "hypotensive" drug (usually veratrum), they were started on a total of 1 to 4 (average of 2) tablets of Serpina* by mouth a day, usually in two doses (morning and night). Observations of blood pressure, pulse rate and general symptomatology were recorded at each visit (usually at weekly intervals), and, when indicated, studies such as electrocardiographic, renal or fluoroscopic were repeated. The drug was given in continuous, not in interrupted courses as in India. *Veratrum viride*, as "Veriloid,"† was usually administered in the maximum dosage tolerated by the patient (8 to 20 mg. a day in four divided doses), and hydrazinophthalazine‡ was given in gradually increasing doses (starting with 50 mg. and working up to 800 mg. a day in four divided doses).

When Serpina alone caused the blood pressure to fall below 150 systolic, 90 diastolic, placebos were sometimes substituted but no other drug was added. Otherwise, after six to ten weeks of treatment

Table 3. *Effects of Serpina and Hydralazine in 17 Additional Patients.*

Patient	Age	Sex	Control Observation			Observation on Serpina Therapy			Observation on Serpina and Hydralazine Therapy		
			Duration of observation	Blood pressure	Pulse	Duration of therapy	Blood pressure	Pulse	Duration of therapy	Blood pressure	Pulse
	yr.		wk.		beats/min.	wk.		beats/min.	wk.		beats/min.
A. G.	44	F	3	170/90	64	8	175/95	61	12	135/75	60
M. H.	51	F	4	220/115	71	12	210/110	68	2	210/110	74
J. K.	34	F	6	190/120	79	6	180/105	72	20	180/105	85
K. McG.	50	F	6	210/120	72	12	165/110	57	13	135/85	68
E. K.	51	F	26	210/110	72	6	210/95	75	4	190/100	82
E. B.	41	F	3	170/110	88	31	155/95	72	16	135/90	72
A.B.	45	F	8	230/150	90	24	170/100	60	18	135/80	76
K. S.	61	F	4	200/100	70	—	—	—	10	180/90	64
E. B.	49	M	100	240/140	72	—	—	—	12	165/85	60
H. F.	47	M	16	170/100	80	24	150/85	68	24	130/75	65
E. A.	58	M	3	210/115	78	—	—	—	12	170/90	78
C. F.	47	F	2	220/130	88	—	—	—	4	180/110	72
D. A.	58	F	3	250/120	68	—	—	—	16	170/90	60
M. B.	45	F	3	190/110	90	—	—	—	32	130/80	72
L. G.	62	F	2	230/110	75	—	—	—	8	190/85	65
H. S.	70	M	2	190/110	90	2	185/110	78	4	160/90	84
M. G.	66	F	8	210/110	72	2	180/100	64	4	155/90	78

Table 4. *Effects of Serpina, Hydralazine and Veratrum Viride in 18 Additional Patients.*

Patient	Age	Sex	Control Observation			Observation on Serpina Therapy		
			Duration of observation	Blood pressure	Pulse	Duration of therapy	Blood pressure	Pulse
	yr.		wk.		beats/min.	wk.		beats/min.
R. D.	48	M	4	170/100	64	8	170/90	60
W. M.	54	M	156	210/130	72	8	195/105	70
R. W.	54	F	22	215/105	92	6	200/95	69
W. G.	62	M	2	230/130	80	—	—	—
B. S.	43	F	1	230/140	85	—	—	—
B. A.	49	M	2	180/125	110	—	—	—
D. C.	34	F	12	195/120	110	4	140/90	94
M. H.	46	F	6	195/110	78	4	165/100	66
I. P.	32	M	156	175/110	70	4	160/90	60
S. M.	51	F	4	150/100	68	—	—	—
C. N.	30	F	4	190/120	100	—	—	—
H. C.	53	F	5	200/120	80	—	—	—
I. B.	51	F	8	250/150	100	—	—	—
C. F.	22	M	24	180/110	70	—	—	—
V. V.	34	F	12	170/105	95	—	—	—
G. C.	45	F	12	215/120	75	—	—	—
R. D.	51	F	4	195/110	75	—	—	—
R. O.	43	F	4	170/105	80	8	140/85	87

*Manufactured by the Himalaya Drug Company, Bombay, India; obtained through the courtesy of E. R. Squibb and Sons, New York City.

†Available from Riker Laboratories, Incorporated, Los Angeles, California.

‡Available from Ciba Pharmaceutical Products, Incorporated, Summit, New Jersey.

without a reduction of pressure to below that level, one of the other two drugs was added, and if the pressure still did not return to normal within another six weeks, the third drug was added. It was found that a considerable number of patients required the combination therapy to bring the blood pressures to normal, if such a reduction could be achieved at all. However, it is not the purpose of this paper to stress the combination medical treatment of hypertension, which will be presented in detail elsewhere.[6, 7]

Results

General

Serpina has now been given to over 100 patients for periods of a month to a year. On the basis of this experience it is possible to make a number of general statements:

In an oral dosage 1 to 3 Serpina tablets a day are well tolerated for weeks and months.

Its action is slow to appear (three to six days) and to disappear (seven to twenty-one days); its chronic effects may not be fully apparent in less than six weeks.

It produces no serious side effects.

It causes sedation, and usually improves sleep, although occasionally it causes nightmares.

It causes bradycardia.

It causes nasal congestion.

It promotes a moderate hypotension, particularly in labile patients with hypertension and tachycardia.

It tends to promote a gain in weight.

It occasionally changes the bowel habit to one of slightly increased frequency.

It apparently does not cause tolerance.

It apparently is not habit forming; administration may be easily stopped for several days to relieve any unpleasant side effects.

It is most useful as an adjunct to more powerful hypotensive drugs.

Specific

Tables 1 to 4 show the responses of 59 patients followed sufficiently long and closely to allow a fair appraisal of the results. The blood-pressure and pulse-rate readings represent the averages obtained before and after treatment for the period noted. In general, the various combinations of drugs were given after trials of single drugs but not necessarily in the same sequence as shown in the tables. It is apparent from the tables that Serpina alone is a hypotensive agent of but modest potency and is usually incapable of reducing the blood pressure to within the normal range except when it is only moderately elevated. The drug is more effective in young, labile (neurotic), hypertensive patients with tachycardia than in those with long established, fixed hypertension with organic vascular disease (these patients usually require combination treatment).

In 13 of the 39 unselected cases in which the drug was tried alone the blood pressure could be controlled within the normal range (150 systolic, 90 diastolic, or lower). However, the average level during the control period in these 13 patients was only 173 systolic, 107 diastolic. The average blood pressure in the entire group of 39 patients before treatment was 192 systolic, 112 diastolic, and the pulse rate 82, whereas after treatment with Serpina alone the levels were 165 systolic, 95 diastolic, and 70 respectively. This compares

Table 4 (*Concluded*).

Patient	Observation on Serpina and Veratrum Viride Therapy			Observation on Serpina and Hydralazine Therapy			Observation on Serpina, Hydralazine, and Veratrum Viride Therapy		
	Duration of therapy	Blood pressure	Pulse	Duration of therapy	Blood pressure	Pulse	Duration of therapy	Blood pressure	Pulse
	wk.		*beats/min.*	*wk.*		*beats/min.*	*wk.*		*beats/min.*
R. D.	4	180/100	56	8	170/100	60	12	150/85	70
W. M.	12	175/95	60	5	190/105	69	4	150/80	63
R. W.	20	195/90	61	4	175/85	64	9	170/80	72
W. G.	—	—	—	6	215/120	90	18	190/100	68
B. S.	4	200/120	70	24	180/110	80	6	180/110	80
B. A.	2	170/110	72	8	144/96	84	12	150/95	75
D. C.	—	—	—	—	—	—	7	120/65	78
M. H.	10	155/90	66	—	—	—	18	160/90	69
I. P.	4	160/95	61	—	—	—	20	150/90	64
S. M.	—	—	—	—	—	—	12	125/80	70
C. N.	—	—	—	—	—	—	12	140/90	76
H. C.	15	175/95	64	—	—	—	12	140/75	64
I. B.	24	190/110	72	—	—	—	24	135/85	76
C. E.	—	—	—	—	—	—	23	105/60	68
V. V.	—	—	—	—	—	—	12	125/72	76
G. C.	16	155/90	73	—	—	—	6	140/80	65
R. D.	—	—	—	—	—	—	3	145/75	72
R. O.	20	145/90	82	—	—	—	4	125/70	83

favorably with placebo treatment in 27 patients, whose blood pressures during the control period averaged 196 systolic, 115 diastolic, but on placebos averaged 186 systolic, 111 diastolic, whereas their pulse rates averaged the same (84). On cessation of the drug, or placebo substitution, the blood pressure usually rose, but not promptly. One physician patient observed that it took four weeks after cessation of dosage for his pressure to resume pretreatment levels. In another case there was no rise in one week but a definite rise, though not to pretreatment levels, during two weeks in which the drug was withheld; after that time it was reinstituted.

In combination with the other two drugs Serpina (Tables 2, 3 and 4) was also well tolerated and appeared to add definitely to their hypotensive effects. Thus, several patients who had been raised to the maximum dosage of *Veratrum viride* that they could tolerate without nausea, had a greater fall in blood pressure, occasionally associated with nausea and vomiting, when given Serpina in addition. By a slight reduction in the dosage of *Veratrum viride* the emetic symptoms were controlled, whereas the hypotensive response was usually maintained.

Similarly, a number of patients given hydrazinophthalazine alone with only moderate hypotensive effects had a definite further reduction of blood pressure when Serpina was added. Except for nasal congestion, Serpina appeared to reduce the side effects of hydrazinophthalazine, particularly the palpitation (tachycardia) and headache usually caused by this drug. We have been impressed with the favorable clinical effect of Serpina combined with hydrazinophthalazine even in patients with chronic and moderately severe hypertension. In 23 cases the average blood pressure was 206 systolic, 116 diastolic, before treatment with this combination and 166 systolic, 93 diastolic after treatment.

When patients failed to respond adequately on a combination of Serpina and hydrazinophthalazine or *Veratrum viride*, they were tried on all three drugs together (Table 4), often with a further reduction of blood pressure. In 18 such patients the average blood pressure was 195 systolic, 117 diastolic, during the control period, and 144 systolic, 82 diastolic, during treatment with all three drugs. Thirteen of these 18 patients were controlled within the normal range; in these cases the average pressure during the control period was 189 systolic, 115 diastolic.

Discussion

Serpina adds another to the rapidly increasing number of drugs which have been tried in hypertension with favorable results in about a third to a half of the cases. Although its chemistry and pharmacology are not completely worked out, it appears to be different from many of the other agents currently being tried. It does not cause postural hypotension and therefore is not regarded as a "blocking" drug, although the nasal stuffiness and bradycardia that it produces suggest a central "sympatholytic" effect resembling that of the dihydrogenated ergot alkaloids. It has a definite sedative effect. Our initial impression was that this might be the main action, but after more than a year's experience, we have come to regard its sedative effect as coincidental. For example, 1 patient had one of his periodic anxiety episodes after being on the drug for a number of months, although he had no rise in blood pressure. In some cases the sedative effect may be undesirable since it is the most common reason for limiting the dosage.

Symptomatic improvement, always difficult to evaluate in hypertensive patients, was so dramatic in some cases that it should be mentioned. A sense of relaxed well-being, decrease in irritability, "improvement in personality" and relief of headache, fatigue and dyspnea were so frequently described by patients that these benefits could not be ignored. Currently, a "double blind" study[8] in which neither physician nor patient knows the content of pills being administered indicates that these symptomatic benefits are quite real, and perhaps the most easily identifiable effects of the drug.

The bradycardia produced by the drug is one of its most definite objective effects. Preliminary observations suggest that the bradycardia is not due to vagal hyperactivity since intravenous injection of atropine appears not to abolish it. Bradycardia may be particularly desirable in some hypertensive patients who habitually have tachycardia or in whom it develops during hydrazinophthalazine therapy.

Nasal congestion and, in rare cases, easy nasal bleeding suggest that the drug dilates the vasculature of the nasal mucous membranes. Patients usually attribute this symptom to a chronic cold, but in some it is bothersome enough to make them try nose drops for relief. There is no adequate explanation for the gain in weight that many patients experience. There is clinical evidence that the basal metabolic rate is not changed but rather that patients are merely more relaxed and less active, sleep better and longer, and perhaps eat as much if not more on the drug than before. A few patients noted extraordinary dreams or nightmares during therapy, but these were relieved by a reduction in the dose or cessation of therapy altogether for several days.

Summary and Conclusions

The moderate hypotensive and symptomatically beneficial effects of *Rauwolfia serpentina* in hypertensive patients are confirmed.

A striking additive if not synergistic effect of this drug in combination with hydrazinophthalazine and with *Veratrum viride* is described.

The drug is well tolerated for months; it produces few side effects, and none of serious consequence. Worthy of emphasis are bradycardia, nasal congestion, sedation and tendency to gain weight.

This drug represents a distinct addition to the pharmaceutical armamentarium against hypertension. It deserves more clinical, chemical and pharmacologic study.

We are indebted to Dr. Meyer H. Halperin for permission to include data on 10 of his private cases in Table 1.

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ARTHRODESIS OF THE ANKLE JOINT*

Indications, Operative Technic and Clinical Experience

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THE ankle joint — to function properly — must have smooth articular cartilage, proper weight-bearing alignment, intact supporting ligaments and good musculature under adequate voluntary control. A variety of pathologic changes are of frequent occurrence. Trauma, infection and certain other processes may cause such damage to the cartilaginous surfaces of the joint that a painful arthritis prevents normal function. Gross deformities of the foot — congenital or acquired — such as a clubfoot or the late sequelae of poliomyelitis and hemiplegia result in inability to place the sole of the foot flat on the floor and to carry out, in walking, the normal motions of dorsal and plantar flexion. Instability of the ankle, caused by muscular weakness or by relaxed supporting ligaments, adversely affects function of the lower extremity in standing, walking and running.

Treatment of these problems by arthroplasty of the ankle joint has, with an occasional exception, yielded disappointing results, and this procedure is rarely to be recommended. Arthrodesis, on the other hand, gives excellent results and is useful in a wide variety of affections of the ankle. Pain due to intra-articular lesions is relieved, deformity and instability are corrected, and the compensatory mobility of the sub-talar and mid-tarsal joints permits a surprisingly free range of foot motion after fusion of the ankle joint. An occasional patient with solid arthrodesis of the ankle has been found at end-result study to have practically no disability and to be able to stand, walk, run or jump in normal fashion. In a report published in 1947 attention was called to the value of ankle arthrodesis in a variety of conditions.[1]

The present study was undertaken in an effort to define more precisely the indications for and the end-results of ankle fusion. We have reviewed our experience at the Massachusetts General Hospital in a five-year period, 1947–1951 inclusive. Fifty-five feet in 50 patients (5 bilateral cases) have been operated upon and form the basic material for this report (Table 1).

Table 1. *Arthrodesis of the Ankle, Massachusetts General Hospital (1947-1951).*

Diagnosis	No. of Cases
Old poliomyelitis	23 (3 bilateral)
Traumatic arthritis — old fracture	11
Nerve or nerve-root injury:	
After disk surgery	3
Peripheral-nerve (peroneal) damage	2
Traumatic paraplegia	1
Spastic hemiplegia	2
Multiple sclerosis	1
Osteomyelitis, septic arthritis	2
Congenital clubfoot	2 (2 bilateral)
Rheumatoid arthritis	1
Osteochondritis	1
Degenerative joint disease	1
Total	50 (55 ankles)

Poliomyelitis (23 cases), old fractures of the ankle with traumatic arthritis (11 cases), and peripheral-nerve or root damage (6 cases) were the most common etiologic diagnoses in this series. Pain, deformity and reduced ability to stand and walk were the common complaints. In several cases the operation was performed to enable the patient to discard a brace.

Operative Technic

It is not particularly difficult to obtain solid bony fusion of the ankle joint, and there are numerous

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variations in operative technic that may appeal to individual surgeons. We prefer to work in a bloodless field produced by application of an Esmarch bandage under moderate tension, beginning at the toes and extending up to the midcalf to express all blood from the veins. Four or at the most five superimposed turns of the same rubber bandage are taken at the midcalf. This is ample to occlude the arterial flow at this level. The distal bandage is then removed. We have never seen ill effects from the use of a tourniquet applied in this fashion.

It is essential that adequate exposure of the whole ankle joint be obtained so that all articular cartilage,

FIGURE 1. *Preoperative Deformity in a Thirty-Three-Year-Old Man Who Had Had Poliomyelitis at the Age of Three, with Resultant Fixed Equinovarus of the Left Foot.*

including that on the malleoli, can be removed. We usually employ two skin incisions, one of which is relatively short and just anterior to the fibula through which the cartilage on the external malleolus and the lateral aspect of the talus is removed. A second medial incision, 10 to 15 cm. long, is made directly over the anterior tibial tendon. Its sheath is incised, and the tendon is retracted. The incision is deepened through the capsule of the ankle joint, and the distal tibia is exposed subperiosteally. After removal of all cartilage from the tibia, internal malleolus and talus, the bony surfaces are shaped so as to produce an accurate fit, and a graft cut from the tibia is placed across the joint line. Additional bony chips are packed in the margins of the joint, the wound is closed in layers, and the ankle is immobilized in a plaster cast extending from the toes to the groin with the knee flexed about 20° and the foot in the preselected position.

The foot should be in neither varus nor valgus, and the central longitudinal weight-bearing axis of the tibia should pass through the axis of the third metatarsal bone of the foot. It is a serious error to allow the foot to remain laterally displaced. Functional results will not be satisfactory in such cases chiefly owing to painful strain of the longitudinal arch. The position regarding plantar flexion of the foot should be carefully chosen. The best functional results have been obtained when the position is between the limits of an exact right angle and 15° of plantar flexion. In male patients with paralysis of the anterior muscle group of the leg the optimum position is an exact right angle. Compensatory motion in the other joints allows weight bearing both barefooted and in the conventional shoe. If all muscles are present and functioning the foot should be set in about 5° of equinus. In female patients 5 to 15° of equinus will permit the use of a heel of medium height. It is seldom advisable to place the foot in marked equinus even if shortening of the leg is present. The rare patient with the knee on the same side fused in flexion should have the ankle fused in neutral flexion or slight dorsiflexion so as to permit the toes to clear the ground in the swing phase of walking.

The portion of the cast above the knee is discarded in about six weeks. A walking heel is applied to the cast, and the patient is allowed full weight bearing as symptoms permit. The walking cast is usually removed in about ten to twelve weeks after operation, and weight bearing is begun in an ordinary shoe with a heel of proper height. An

FIGURE 2. *X-Ray Films before and after Operation in Patient Shown in Figure 1.*
The cosmetic and functional results are excellent.

elastic bandage or stocking should be worn until post-immobilization edema subsides.

In patients who have had a dislocation of the talus with resultant aseptic necrosis of this bone and in those who have had a previous triple arthrodesis of the foot, the circulation of the talus is so impaired that the usual operative technic to produce fusion is likely to fail. In such cases through a lateral incision we remove the distal 10 cm. of the fibula, square it with the motor saw and countersink it into a bed cut in the lateral aspect of the tibia, talus and os calcis, fixing the graft to these bones with screws. These operative procedures for

obtaining ankle fusion are not original with us, and have been described in detail elsewhere.[2, 3]

Discussion

Poliomyelitis

Poliomyelitis produces a wide variety of disabling conditions of the foot and ankle. Foot drop

Figure 3. *X-Ray Films in K. M., a Forty-Two-Year-Old Woman Who Had Had Poliomyelitis at the Age of Sixteen, with Almost Complete Paralysis of All Muscles below the Knee. The preoperative film shows 90° equinus deformity of the foot. X-ray film taken 8 weeks after operation shows the degree of correction obtained. The cosmetic and functional result four years later was excellent.*

is most often due to paralysis of the toe extensors and anterior tibial muscles. If the onset of poliomyelitis is in childhood, muscle imbalance, faulty

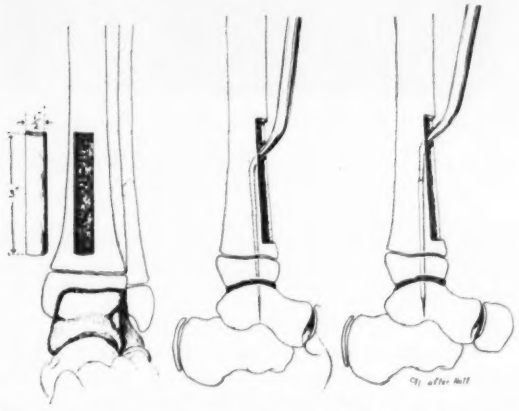

Figure 4. *Diagram Showing Ankle Fusion by the Hatt Method.*

function and impaired circulation may cause severe deformities of the foot of any type, with accompanying distortion of the bony architecture. If the disease develops after full growth has been attained, the intact ligaments and strong skeletal structures prevent the development of severe deformities. In adults with foot drop or complete involvement of the muscles controlling the foot, ankle arthrodesis gives satisfactory results (Fig. 1–3).

In the growing child, ankle arthrodesis should be undertaken only after careful consideration of many factors. In all cases of foot drop in which muscles suitable for transplantation are present, triple arthrodesis and muscle transplant yield superior results. In cases in which active power in dorsiflexion cannot be gained by stabilization and muscle transplant, ankle fusion may be the operation of choice. The following case is of interest:

Poliomyelitis developed in R. R., a 5½-year-old boy, with almost complete paralysis of all muscles below the left knee and marked weakness of the thigh musculature. A short brace to stabilize the ankle caused excessive knee strain. To enable him to discard the apparatus an ankle fusion was done

Figure 5. *X-Ray Film of the Foot before Operation.*

in 1948 by the method of Hatt (Fig. 4) at the age of 7. Figure 5 shows the preoperative x-ray appearance of the foot, and Figure 6 the immediate postoperative appearance. Two sets of bone markers were placed so that growth at the distal tibial epiphysis could be accurately measured. A marker was placed at each end of the graft, and a second set of markers placed in the tibial cortex proximal and distal to the epiphyseal plate. At follow-up examination 3 years after operation the foot was in excellent weight-bearing position, and the gait was good. The patient used no brace. X-ray films (Fig. 7) showed the ankle to be solidly fused. The distal epiphysis of the tibia was still open, and both sets of markers had separated 1.5 cm., indicating that growth was occurring at this epiphysis. The bone graft had completely lost its identity as a separate structure.

End results were ascertained in 20 cases of poliomyelitis with ankle fusion. Eleven patients were found to have excellent and 7 were found to have good results. Thus, a total of 18 of the 20 patients had satisfactory results after ankle fusion. Of the other 2 patients 1 had a fair result, and 1 was rated poor. In the case with the poor result the ankle fusion had to be supplemented at a later date by triple arthrodesis because of excessive foot instability. It should be noted that 1 patient with bilateral ankle fusion had an excellent result.

Fractures

Fractures with malunion or dislocations involving the ankle may produce pain and disability, often of marked severity. The most satisfactory method of treatment of such cases is arthrodesis of the ankle, which relieves pain, corrects malalignment and restores ability to stand and walk on level surfaces. Roofers, painters and others who stand on uneven or sloping surfaces may be unable to return to full preinjury activity, but there is surprisingly little disability from an ankle fusion if the

FIGURE 6. *Appearance of the Foot on X-Ray Examination Immediately after Operation.*
Markers in the graft, 4.4 cm.; markers in the tibia, 1.7 cm.

musculature is normal. One patient has returned to work as a professional skier and ski instructor with a fused ankle. The operation was necessary because of a severe traumatic arthritis after a fracture that occurred in skiing.

If an ankle fracture is subjected to open reduction and postoperative sepsis occurs, complete disability may result until ankle fusion is performed, as in the following case:

A. O., a 60-year-old woman, sustained a trimalleolar fracture in 1949; attempts at closed reduction were unsuccessful. Open operation was done, and severe postoperative sepsis occurred. When the patient was first seen about 1 year after operation, a draining sinus was present posterior to the ankle joint, the foot was extremely painful, and partial weight bearing was possible only with the aid of crutches. X-ray examination revealed a large area of decreased density in the distal tibia, which represented an active focus of infection. At operation the sinus tract was excised, and all dead bone and granulation tissue were removed, as was the cartilage of the ankle joint. No graft was used. The denuded bony surfaces united, the sinus closed promptly, solid fusion has been obtained, and the patient has an excellent functional result.

Our experience with ankle fusion for painful malunion has been so favorable that we have no hesitance in recommending it as the treatment of choice in such cases.

Foot Drop Due to Peroneal-Nerve and Intervertebral-Disk Lesions

A protruded intervertebral disk in an occasional case produces foot drop or flail foot because of pressure on nerve roots. Unless the pressure is promptly relieved the damage is irremediable. Manipulation of nerve roots in operative removal of a protruded disk occasionally produces a similar lesion. In such cases a brace, active exercises and physical therapy are prescribed. If no recovery occurs in a year, arthrodesis of the ankle may enable the patient to discard the brace and to wear ordinary shoes. We have had 3 such cases in this series. Peripheral peroneal-nerve lesions from foot drop may also be successfully treated by ankle fusion, but the patients with progressive disabilities, such as muscular dystrophy, multiple sclerosis and syringomyelia, should be treated conservatively rather than by operation. One patient with multiple sclerosis and 1 with rheumatoid arthritis treated by ankle fusion

FIGURE 7. *X-Ray Appearance of the Foot Three Years after Operation.*
Markers in the graft, 5.9 cm. (1.5 cm. increase); markers in the tibia, 3.2 cm. (1.5 cm. increase).

attained little benefit, since the relentless progress of the disease soon prevented anything but a wheelchair existence.

SUMMARY AND CONCLUSIONS

Our experience with ankle fusion in fractures, in certain irreparable nerve lesions, in joint infections and in poliomyelitis has been most satisfactory. In properly selected cases the results have been gratifying to the patient and to the surgeon. The operation is established as an integral part of our armamentarium.

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THE EFFECT OF INTRAVENOUS INJECTION OF EMULSIFIED VITAMIN K_1 ON THE HYPOPROTHROMBINEMIA INDUCED BY TROMEXAN*

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TROMEXAN (ethyl biscoumacetate; 3, 3′ carboxymethylenebis- [4-hydroxycoumarin] ethyl ester also known as B.O.E.A., D.E.A. and Pelentan) has been proved to be an effective agent for inducing hypoprothrombinemia. After synthesis of the drug in 1948 by Reinis and Kubik,[1] many investigators reported favorable clinical results. Severe hemorrhages, however, have followed its use.[2-4] Since Vitamin K_1 has been shown to be of value in reversing the hypoprothrombinemia induced by Dicumarol,[5] it seemed possible that it would prevent catastrophes resulting from Tromexan therapy. The purpose of the present paper is to report observations on this point.

MATERIALS AND METHODS

For the purpose of the study Tromexan was administered to 18 patients. Indications for anticoagulant therapy are listed in Table 1. It will be noted that dosages required to obtain a "therapeutic" plasma prothrombin level of 10 to 30 per cent were slightly higher than those reported in the literature.[2, 6-12] Initial doses were between 1.5 and 2.1 gm., and maintenance daily dosages varied from 0.6 to 2.1 gm. At the end of sixteen hours the prothrombin activity was consistently below 50 per cent of normal, and at the end of thirty-six hours it was in the "therapeutic" range.

Of the 18 patients in whom hypoprothrombinemia was induced and maintained by Tromexan, 10 were given Vitamin K_1 intravenously to observe the speed of return of the plasma prothrombin level to normal. The Vitamin K_1 used in the study‡ was the purified, naturally occurring fat-soluble compound (2-methyl-3 phytyl-1-4-naphthoquinone) identical with that originally identified from alfalfa by Dam and his associates.[13] The preparation, in the form of an oil, was emulsified by the addition of emulsifying agents for purpose of intravenous administration by the Department of Nutrition of the Harvard School of Public Health. The emulsion contained 50 mg. of Vitamin K_1 per cubic centimeter, and the dosage was 5 mg. per kilogram of body weight. The administration was by the intravenous route, the first cubic centimeter being given slowly over a two-minute period to avoid

TABLE 1. *Indications for Coagulant Therapy.*

CASE NO.	PATIENT*	AGE	PRIMARY DIAGNOSIS	INDICATION FOR ANTICOAGULANT THERAPY	DRUG USED AFTER DISCONTINUANCE OF TROMEXAN
		yr.			
1	J. L.	50	Recurring phlebitis, deep, left leg	Thrombophlebitis, acute	Vitamin K_1
2	E. M.	56	Carcinoma of anus	Ileofemoral thrombophlebitis	Vitamin K_1
3	J. C.	51	Fracture, left femur	Pulmonary infarction	Vitamin K_1
4	H. N.	52	Duodenal ulcer	Rise in platelets after splenectomy	Vitamin K
5	J. K.	55	Recurring phlebitis	Acute thrombophlebitis	Vitamin K_1
6	C. C.	30	Postphlebitic syndrome	Acute chemical phlebitis	Vitamin K_1
7	J. C.	26	Buerger's disease	Acute thrombophlebitis	Vitamin K_1
8	F. C.	28	Appendectomy	Pulmonary infarction	Vitamin K_1
9	H. B.	55	Multiple arterial emboli	Acute femoral-artery occlusion from heart (myocardial infarct)	Vitamin K_1
10	E. B.	30	Herniorrhaphy	Acute ileofemoral thrombophlebitis	Vitamin K_1
11	P. C.	41	Duodenal ulcer	Rise in platelets after splenectomy	Synkayvite
12	A. S.	33	Postphlebitic syndrome	Acute thrombophlebitis	Synkayvite
13	W. M.	40	Duodenal ulcer	Rise in platelets after splenectomy	None (control)
14	R. B.	42	Gastric ulcer (benign)	Acute thrombophlebitis	None (control)
15	J. Q.	63	Myocardial infarction	Prevention of pulmonary infarct	None (control)
16	T. O'L.	38	Buerger's disease	Acute thrombophlebitis	None (control)
17	H. C.	53	Recurring phlebitis	Acute thrombophlebitis	None (control)
18	M. S.	55	Myocardial infarction	Prevention of pulmonary infarct	None (control)

*All patients were men.

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‡Kindly supplied by Merck and Company, Rahway, New Jersey.

pyrogenic reaction, and the remainder over a total of fifteen minutes.

In 2 additional patients Synkayvite (2-methyl 1,4-napthohydroquinone 3-sodium sulfonate), one of the many water-soluble naphthoquinones having strong Vitamin K activity, was used intravenously in single 15-mg. doses to compare its effect with that of Vitamin K_1. The 6 remaining patients were used as controls, no antagonist being given and the Tromexan effect being allowed to disappear without interference.

The Vitamin K_1 or the Synkayvite was given only after a stable level of hypoprothrombinemia had been produced with Tromexan. The injections were administered in all cases sixteen hours after the last dose of Tromexan had been given.

Results with Vitamin K_1

In all 10 patients who were given the emulsion of Vitamin K_1 there was a demonstrable elevation of prothrombin activity (Fig. 1). Three hours after the drug was given and sixteen hours after the last dose of Tromexan the prothrombin activity was twice its original level and outside the therapeutic or dangerous range. Twenty-four hours after administration it averaged 73.2 per cent (range, 46 to 95 per cent). No untoward effects were observed from the administration of the emulsified Vitamin K_1 by this method.

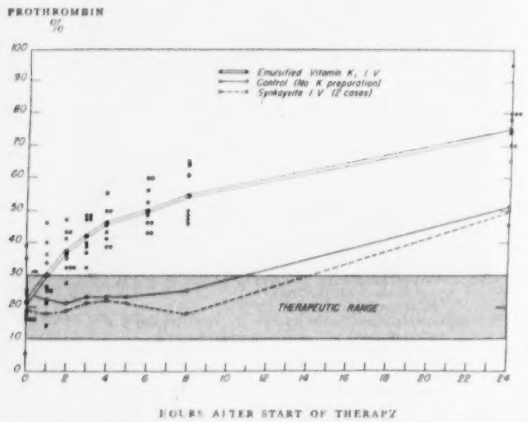

Figure 1. *Effect of Vitamin K Preparations on Hypoprothrombinemia Caused by Tromexan.*

The words "hours after start of therapy" pertain to the number of hours after the emulsified Vitamin K_1 or Synkayvite was injected. This was sixteen hours after the last dose of Tromexan.

In the control series of 6 patients who were given no Tromexan antagonist the prothrombin activity, after discontinuance of Tromexan, returned gradually to normal (Fig. 1). Eight hours after the "start" of therapy (Fig. 1), or twenty-four hours after the last dose of Tromexan, the prothrombin activity was still depressed in the "therapeutic" range, and forty hours after the last dose of Tromexan had been given the mean prothrombin activity was 53.5 per cent (range, 18 to 74 per cent).

In 2 patients 75 mg. of synthetic Vitamin K (Synkayvite) was given intravenously. The results in these cases were not so favorable as those in which Vitamin K_1 was given and not unlike the response in the patients given nothing at all (Fig. 1).

Discussion

The observations show that the antagonistic effect of intravenous administration of emulsified Vitamin K_1 on the hypoprothrombinemia produced by Tromexan is approximately the same as the effect on the hypoprothrombinemia produced by Dicumarol[5] and Phenylindandione.[14]

We were also interested to observe in 2 of the patients treated with Vitamin K_1 after Tromexan, just as in the patients so treated after Dicumarol, a relative resistance to subsequent immediate administration of the drug concerned. Both patients required approximately twice the dose (1.8 to 2.1 gm.) of Tromexan for therapeutic hypoprothrombinemia to be produced a second time.

Summary

Vitamin K_1 in fat emulsion, given intravenously, proved to be an effective antagonist against the hypoprothrombinemia induced by Tromexan in all of 10 patients studied. The response was similar to that seen in the hypoprothrombinemia induced by Dicumarol.

Emulsified Vitamin K_1 appeared more effective than the synthetic water-soluble Vitamin K preparation, Synkayvite, in restoring prothrombin concentrations toward normal.

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MEDICAL PROGRESS

PSYCHOSURGERY (Concluded)

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GENERAL CONSIDERATIONS OF RESULTS

As lobotomy has spread to more and more centers, the general conviction is strengthened that this method is capable of modifying disturbed behavior of psychotic patients. Small as well as large series carry the same message. Indeed, authors who express over-all disappointment are few and far between. A partial list is given here of workers who have described their experience since 1948.

Jones and McCowan[97] reported 12 cases with "periodic" psychosis, including 9 catatonic and 3 manic depressives, followed for an average of three years and six months. The patients had an average of fourteen years of illness. Five recovered, 5 were markedly improved, 1 was slightly improved, and 1 was worse. Periodic psychosis was considered eminently suited for leukotomy. Stevenson and Geoghegan[75] presented a follow-up study of 9 patients with frequent or continuous manic-depressive attacks so that continuous hospitalization was necessary; 7 left the hospital. Stevenson and Wilson[98] studied 23 manic depressives; after lobotomy, 21 were able to leave the hospital, 13 being considered "Grade A" recoveries. Most of their patients gained 30 to 50 pounds in weight.

The experience of Winnik and Askenazy[99] was with 18 psychotic cases operated on by the Freeman–Watts approach; 6 were much improved, and returned to their former occupations, and 7 were somewhat improved. Wiederlight,[100] at Delaware State Hospital, reported 32 cases with poorer than average results, although 8 patients were able to live at home, and 5 were able to work. Carscallen et al.[85] studied 49 cases in a Veterans Administration hospital followed for six months, and reported generally a rise above preoperative level of adjustment with no great damage to intellectual functions. Durand[101] described amelioration of symptoms in 10 of 15 patients with no definite impairment of intellectual capacities. Tompkins[102] described 36 patients with chronic mental illness operated on by Mixter at the McLean Hospital. All but 2 patients were improved, only 3 had troublesome traits such as incontinence, obscene behavior, combativeness and silliness. Four patients who had been given electric shock or Metrazol before operation suffered epileptic convulsions, but these were only single seizures.

Larger series (50 to 100 cases) have been reported by Ehrenberg and Johnson,[103] de Greeff and Ectors,[104] Drubin[105, 106] and Rosie.[107] Ehrenberg and Johnson have divided their 71 cases at the Boston State Hospital into integrated and disintegrated patients with schizophrenia, and report a marked difference in outcome for the two groups — the former showing an improvement rate of 82 per cent, and the latter 8 per cent. This is obviously a useful prognostic distinction, in a class with "emotional tension" as a predictive sign. Two thirds of the patients discharged were partly or completely dependent upon others for economic support or supervision. This was attributed to frontal-lobe defect, rather than illness, since symptoms of psychosis were essentially removed. DeGreeff and Ectors reported on 60 leukotomies (including bilateral and right unilateral operations). The series comprised 30 psychotic, essentially schizophrenic patients, and 30 nonpsychotic patients, essentially cases of anxiety and psychoasthenia. The results, on the whole, were favorable, but with wide variations. A postleukotomy dementia, as well as an infantilism manifested in the emotional sphere and in the higher intellectual processes, was described.

Drubin reported on 62 veterans followed for four months to three and a half years after lobotomy. Marked improvement was recorded in 37 per cent, with 6 discharged, 12 on trial visit, and 5 given ground privileges; moderate improvement occurred in 29 per cent, slight improvement in 27 per cent and no improvement in 7 per cent. Three patients who relapsed postoperatively after significant improvement were given electric shock and improved again. Postoperative *grand-mal* seizures occurred in 19.4 per cent of cases; all had abnormal electroencephalograms, and all attacks were controlled by Dilantin. Drubin noted that the percentage of discharge or trial visit did not truly reflect the mental state of the veterans because of the problem of finding relatives to care for them. A second follow-up study of the same group nine months to four years after lobotomy showed 27 per cent markedly improved, 31 per cent moderately improved, 27 per cent slightly improved and 15 per cent unimproved. As the interval between date of operation and date of evaluation increased, the total number of appreciably improved cases tended to decrease, and the number classified as slightly or not improved tended to increase. Only 2 of the patients made a satisfactory occupational adjustment, and only 5 a good social adjustment at the longer follow-up study.

The investigation by Rosie[107] of 68 patients *not* discharged from the hospital is a commendable effort to ascertain the value of lobotomy for the group of patients left behind — almost always the

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larger group in any series. A follow-up study of one to four years revealed that 6 were greatly improved, 10 improved, 28 slightly improved, 20 unchanged and 4 worse. Two thirds of the patients were freed from distressing emotional tension. Hallucinations disappeared in a quarter, were less intense in a half and were unchanged in a quarter of the cases. Thirty patients relapsed after nine months; in 14, the relapse was permanent. Electric-shock therapy, which was given to 46 of the 68 patients postoperatively, cut short isolated impulsive bursts; in 12 cases, it favorably altered the clinical picture in a relapse. Maintenance electric-shock therapy gave a higher level of adaptation in a few cases after operation than was possible before operation. Epileptiform convulsions appeared in 6 patients, all of whom had had electric shock before leukotomy. Voracious appetite was a common symptom, attributed to lack of visceral distress or fullness after an adequate meal, less self-consciousness and less self-criticism. No correlation was found between weight gain and improvement.

A hundred or more cases have been reported by several investigators. Fernandes et al.[82] obtained beneficial results in 70 per cent of 100 cases, with social recoveries in 37 per cent and frank improvement in 12 per cent. There were 8 relapses in six months; 3 patients became well again after electric and 1 after insulin shock. Lyerly[108] reported 76 per cent of patients moderately or greatly improved among 127 cases. Van Coller[109] also obtained improvement in 70 per cent of all chronic incurable psychotic patients operated on, with a mortality of 2 per cent.

Peterson and Love[110] followed 250 patients after prefrontal lobotomy; 38 per cent were dismissed from the hospital, and another 8 per cent could have been dismissed except that there was no home to receive them.

The Connecticut Lobotomy Committee (Friedman, Moore, Ranger and Russman[86] followed 254 patients for two years, as well as 100 controls for whom operative permission was refused. The patients operated on made significant gains, for 37.6 per cent were released, 57.8 per cent showed significant improvement and 54 per cent were able to work, of whom 22 per cent worked full time and 32 per cent part time. There was little change in percentage of improved cases over the two-year period. Controls, by contrast, showed insignificant changes.

Worthing and his associates[77] have investigated changes in 600 patients operated on by the Lyerly technic. Improvement was stable and even progressive, with no late deterioration. After one to four years, a third of all patients operated on were home, and patients remaining in the hospital were generally improved. Spontaneous convulsions did not exert a favorable effect upon the clinical course, although electric-shock-induced convulsions at times favorably affected the clinical course. Releases from hospital were fewer for older patients, the quality of remission was less satisfactory, and the mortality rate was higher. The preoperative response to electric shock was considered prognostic. Chronic hallucinations were an unfavorable preoperative sign.

The Veterans Administration[111] recently collected 1500 cases from 28 centers. Benefit in terms of desirable personality changes did, indeed, occur, but these were not reflected in discharge rates or social or economic independence to the degree reported in other series.

The five-year follow-up study by Greenblatt and Solomon[112] and the ten-year follow-up by Freeman[113] indicate that improvement generally tends to be maintained over the long run. There was not the slightest evidence of a wholesale deterioration or tendency to relapse. Greenblatt and Atwell[19] observed that abstraction capacity tended to fall off over five years, but this was not correlated with either deterioration of mental status or loss in social adjustment.

General Results with Different Types of Operation

Transorbital Lobotomy

Freeman,[113] in 1948, electrified the psychiatric public by his announcement of the use of Fiamberti's transorbital method for treatment of mentally ill patients. He stated that the technic was simple, swift, safe and effective, particularly in patients who had not deteriorated.[114] The fact that a psychiatrist was carrying out this strictly surgical procedure without elaborate aseptic precautions offended many conservative colleagues. Since the status of this method in the therapeutic armamentarium of psychiatrists is still debated, it is prudent to evaluate the procedure as carefully and objectively as possible.

In 1948 and 1949 Freeman[115, 116] reported 100 cases of transorbital leukotomy for mental disorder. There were no deaths; complications developed in only 3 cases. The indications at this time were stated to be for ambulatory schizophrenic patients, subject to remissions and relapses and suffering from severe tension. The procedure was contraindicated for long-standing schizophrenia, for severe emotional deterioration and for intractable pain. In a later report (1949), Freeman[117] reviewed his experience in 350 cases: 2 patients suffered fatal hemorrhage, and 2 died from other causes; the results were still encouraging. At that time, the effects of the deep frontal cut were discussed, Freeman stating that the deep cut was as extensive anatomically, and as effective clinically, as major frontal leukotomy.

The lesions in transorbital leukotomy have been described by Freeman and Williams[117] and by Freeman.[116] Transorbital lobotomy produces minor lesions of the skull and dura. The cortex is usually

traumatized very little. The distinctive changes are within the white matter, the incision severing the thalamofrontal radiation just lateral to the anterior horn of the lateral ventricle, although sometimes penetrating the ventricle and lacerating the caudate nucleus. There is a hemorrhagic cavity in the frontal white matter, which evolves into a cyst with pigmented walls. Wallerian degeneration can be traced into the frontal lobe and also through the internal capsule into the pons. Retrograde degeneration in the thalamus is milder than that seen after prefrontal lobotomy. From the pathological standpoint, transorbital lobotomy is considered to be a clean-cut, selective operation for severing the frontothalamic radiation. The deep cut severs thalamofrontal radiations at a lower level and more in the anteroposterior plane, opposite the head of the caudate nucleus. Occasionally, it penetrates the ventricle, but this appears to be harmless. Occasionally, cerebrospinal fluid or a small quantity of blood escapes; once cerebrospinal rhinorrhea occurred, lasting ten days, but with penicillin being given prophylactically in all cases, complications were rare.

Jones and Shanklin[118] described their experience with 52 patients. At the end of one or two years of follow-up study, 28 patients were out of the hospital, most of them employed; they were less tense, more sociable and more friendly. No convulsions had occurred. It was now possible to establish a psychotherapeutic relation, which had not been possible before surgery. Moore and Winkelman[119] reported similar results in 110 assorted cases; the over-all improvement rate was 61 per cent, 35 per cent making a satisfactory social and economic adjustment outside the hospital. The operation proved best in catatonic and paranoid patients among the schizophrenic group. Affective psychosis and obsessive-compulsive cases showed satisfactory improvement in more than 80 per cent of the cases. One feature emphasized by Moore and Winkelman, as well as others, is the fact that after transorbital operation, electric-shock treatment had a more rapid and lasting effect than before operation.

Wilson et al.[120] studied 200 cases followed for six months after transorbital operation. This group consisted mostly of chronic cases, with an average duration of illness of eleven and seven-tenths years. Of 200 patients, 26 left the hospital, 22 made a fair hospital recovery, and 90 were improved to usefulness. Seventy per cent of the patients needed less supervision. The operative mortality was 1.5 per cent. Wilson and his co-workers also found their patients more amenable to electric-shock treatment after operation.

Edwards[121] followed 52 patients for ten to twelve months, 19 of whom had received the deep frontal cut, which was considered more effective than the original transorbital operation; complications were fewer, and intellectual defects slight. Greatest value was claimed for depressions, anxiety states and hypochondriasis, little value in chronic dementia praecox, and no value in obsessions. The response to electric shock was improved after operation.

Fleming and Phillips[122] obtained satisfactory results in 7 of 8 cases.

Of all who have reported on this operation, only Elder et al.[123] obtained unsatisfactory results, for 8 out of their 11 patients had to be operated on again.

Topectomy

Topectomy, involving bilateral removal of various parts of the frontal cortex according to Brodmann's mapping, was reported in full in a volume by Mettler and his co-authors,[124] who together constituted the Columbia–Greystone workers. The clinical material consisted of 24 psychotic patients whose prognosis was grave, and 24 control patients, psychologically matched, who shared the same environment and work-up before and after the "operative" period and were subjected to Sodium Amytal narcosis and phlebotomy instead of topectomy. Altogether, 17 different operations were carried out, with much overlapping of areas removed.

In the control group, after four months, there were 3 improved, paroled cases. Of the patients operated on, 20 out of 24 were recommended for parole at four months; at the end of a year, 9 were at home, 8 working at their former capacity. Removal of areas 9, 10 and 46 seemed to give the best results, and the junction of areas 9 and 10 seemed to be most satisfactory in relief of painful affect. Excision of areas 6 and 8 was deemed unsatisfactory. Topectomy did not interfere with social, moral or intellectual performance, carefully measured in a large battery of tests. There were no deaths, and complications such as convulsive seizures and incontinence were few.

In other publications, Pool and his co-workers[125-130] stressed the importance of the quantitative factor in treatment. Removal of 30 to 35 gm. of tissue was recommended in psychotic cases and 20 to 25 gm. in cases of pain. The more normal the patient, the less the amount of tissue sacrificed. The results were stated to be as good as those reported for standard lobotomy and for undercutting, and the amount of tissue cut was estimated as about 50 per cent of that cut in standard lobotomy. Of 106 patients reported on in 1951, 40 per cent were significantly improved, and 34 per cent socially rehabilitated. However, longer follow-up study revealed an incidence of 16 per cent of seizures after topectomy. Less personality loss, incontinence and mortality was claimed for topectomy than for standard lobotomy. Pool mentioned 7 patients who had failed to respond to transorbital lobotomy, 3 of whom later responded to topectomy. Another 7 unmanageable and deteriorated schizophrenic patients not improved by topectomy were improved by lobotomy. He did not recommend topectomy over lobotomy for

cases of pain, because of the greater surgical magnitude of the former operation.

Le Beau[131] and Le Beau, Feld and Bouvet[132] operated on 10 patients, 5 children and 5 adults, with anxiety and agitation, excising area 9 and sometimes 10, bilaterally. There was no evidence of intellectual impairment in elementary or complex functions. Behavior, too, suggested psychologic integrity, and affectivity showed improvement with time. Good results were obtained in adults, and in several children. Two of the patients who suffered from epileptic attacks before operation demonstrated no aggravation of the seizure disorder after operation. Hardman[133] reported disappointing results with excision of areas 9, 10 and 13, for of 8 cases with excision of areas 9 and 10, improvement occurred in 1 and in 3 cases with excision of area 13, little or no benefit occurred.

Some critical comment may be introduced here. Although the operation was originated to provide greater precision in localization of tissue cut, the vagueness of Brodmann's boundaries, the lack of cytoarchitectural differences in many areas and the great variations in different brains make this method much less precise than some suppose. The original series of controls, unfortunately, differed from patients operated on in at least two essential respects — in anxiety level and in complaint level, both factors favoring better results in the patients who were operated on. In judging the relative efficacy of topectomy and other available surgical methods, comparative series of cases with operation in the same clinic, are most important. The report of Wayne[134] is helpful in this respect. Cases of topectomy, numbering 20, were compared with 87 cases of standard lobotomy. The rates of improvement after topectomy were considerably below those after lobotomy. In 7 cases lobotomy after ineffectual topectomy was followed by moderate improvement in 3 and slight improvement in 4. The incidence of seizures was higher after topectomy than after lobotomy. The author estimated that the patients were perhaps more severely ill than those included in the original topectomy studies, and concluded that standard lobotomy was preferable to topectomy when emotional and intellectual regression had occurred.

Cortical Undercutting

Cortical undercutting refers to leukotomy in a plane deep to and parallel to gray matter. It is like a topectomy except that the isolated tissue is left in situ. The chief exponents of this method have been Scoville[135, 136] and Scoville and Wilk,[137, 138] who have had considerable experience in three planes: undercutting of areas 9 and 10; undercutting of the inferior orbital cortex; and undercutting of the mesial frontal cortex.

Scoville claims that the orbital operation is best in neurotic patients, the superior operation in cases of intractable pain and addiction and the orbital combined with superior in affective and schizophrenic patients and that the mesial frontal undercutting operation is of research value only. He believes that the undercutting technic, unlike the topectomy operation, severs only a third of the fibers usually cut in the standard operation, and that the blood supply is left relatively intact. The results are stated to be equal to those of the standard operation. Here, again, no adequate comparison of standard lobotomy and undercutting is offered. However, on the basis of a follow-up study of one to twenty months in more than 100 cases, 46 per cent over-all improvement was noted for a chronic group of patients when the orbital surface or the convexity was undercut. Little or no "blunting" of the personality was noted after undercutting, and less disturbance of behavior than after standard operation. The incidence of postoperative seizures was reported as 12 per cent.

Thalamotomy

The chief exponents of this procedure have been Spiegel and his associates.[139-143] This interesting technic is designed to make circumscribed lesions in the thalamic nuclei, the funnel of thalamocortical projection systems. By regulating the strength and duration of current applied, it is possible to make small lesions about 3 mm. in diameter with high precision in discrete areas. In an initial group of cases, only one or two lesions were placed in each dorsomedial nucleus, but no permanent improvement was obtained; later, more lesions were applied, with encouraging results. Recent reports concern 44 patients in whom 62 operations (partial dorsomedial thalamotomy combined with hypothalamotomy in several stages) were performed, with an operative mortality of 3.2 per cent. Circumscribed lesions of the dorsomedial nucleus beneficially influenced emotional disturbances and produced relief from anxiety, tension, depression, agitation and obsessive-compulsive behavior. As with the other psychosurgical procedures, hallucinations and paranoid ideas tended to lose their charge and eventually subsided.

Of 35 patients observed for over six months, 6 were definitely improved and working at or near full capacity; 11 returned home with reduced working ability, and 8 became more manageable in the hospital (7 patients in these two groups relapsed); and 10 were not changed. In some cases in which lesions of the dorsomedial nuclei were insufficient or the improvement was only temporary, small lesions were placed in the posterolateral hypothalamus, and in several cases this resulted in further benefit.

Compared with the operations on the frontal lobes, thalamotomy and hypothalamotomy seemed to have chiefly two advantages: most of the severe personality changes following frontal lobotomy were

avoided; and the formation of extensive cortical scars was obviated. One patient had a single seizure, and electroencephalographic changes generally consisted only of mild transitory slowing, affecting the frontal leads.

Frontal Lobectomy

Peyton and his associates[29] have added to their earlier results with a report of 53 patients, 32 of whom were followed for eight to thirty-six months. These were chronic patients averaging fifteen years in duration of psychosis. Thirty of the 32 patients improved. Almost all showed increased initiative and ability to participate in institutional work and recreational activities. Assaultiveness and soiling were most strikingly relieved; improvement in mental content was rare. One patient had a *grand-mal* seizure after six months.

Cingulate Operation

As noted above, Pool[130] did not obtain encouraging results from bilateral removal of the anterior cingulate gyrus. Hardman,[133] however, carried out excision of area 24 with adjoining area 32 in 7 cases of dementia praecox, with some improvement in 2. Five patients with other diagnoses made social recoveries. Scoville et al.[138] considered undercutting of the cingulate to be less satisfactory than undercutting of either the vertex or the orbital surface. McLardy and Meyer found no special advantages to cingulate operation. Livingston[144, 145] has reported on bilateral cingulate isolation with results regarded as very promising.

Orbital Isolation

Egan[146] has reported on orbital-lobe isolation in 52 cases, in an attempt to preserve the good results usually associated with orbital operations and, at the same time, to avoid epileptic convulsions, which often accompany operation higher up. His patients were chronic cases with average duration of illness of ten years. There were no deaths, and seizures developed in only 2 patients. At eighteen months of follow-up study, 26 patients were out of the hospital; 11 were gainfully employed. In personality, they were happy and carefree, but sometimes rude, inconsiderate, defiant and quarrelsome. Restlessness, aggressive outbursts and hyperactivity were reduced.

Unilateral Lobotomy

Recently, Peterson and Love[110] reported excellent results in 2 patients with involutional psychosis subjected to unilateral operation and advised further consideration of its use in the aged. Prick[147] studied 5 cases of serious refractory psychasthenia followed for three years after a unilateral operation. The intelligence quotient was lowered in all. There was a basic disturbance in the imaginative life; fantasies and dreams were fewer, abstract thought and creativity diminished, judgment and criticism weakened, and sensitivity and emotional responsivity greatly reduced. Simon and his coworkers[148] contrasted 16 unilateral with 16 bilateral cases. Correct guesses were made by observers about the type of operation in almost all cases. Significant improvement was 17.6 per cent after unilateral and 68.8 per cent after bilateral lobotomy. A second operation in 14 unilateral cases resulted in a rise in significant improvement level to 78.6 per cent.

Operations for which little enthusiasm exists include *gyrectomy* (Penfield[72]), *temporal lobotomy* (Obrador[149]) and *parietal lobotomy* (Yahn et al.[150]). The old *Moniz technic* is still being tried in some quarters (Yahn and his co-workers and Fernandes et al.[82]), but its essential place in psychosurgery is historical. *Venous ligation* has been done by Columbia–Greystone workers[59] on 12 patients; after eight months, 2 were slightly improved, 9 were unimproved, and 1 was dead. These workers also studied 2 *thalamotomy* cases (both patients were slightly improved), 2 patients subjected to *thermocoagulation* (both much improved) and 9 patients with *transorbital* operations (2 much improved, 3 improved and 4 slightly improved).

Personality Changes

After psychosurgery patients are represented as unchanged in some respects, improved in others, and worse in still others, so far as socially desirable traits are concerned. Most discussions center about comparisons of the immediate preoperative with the postoperative picture. Few compare the patient's personality before illness with that after operation.

Mossa[151] studied 50 chronic patients and claimed that there was no modification in perception, memory, feeling, reflection, associative faculties or ethical sense. He found no evidence of regression to infantile levels. Cattell[152] stated that the basic personality was not altered, without clarifying the meaning of that very ambiguous term "basic personality."

A great variety of changes that may be considered favorable so far as total adaptation is concerned have been noted. Levine and Albert[153] stated that some obsessive patients who had never experienced sexual gratification because of many inhibitions obtained sexual gratification for the first time in their lives after lobotomy. Heath and Pool[82] found that emotions were more readily and appropriately discharged. Repression with tension did not occur. Tension did not build up. Rage and fear were less, but apparently joy was also less profound. Johnson and Benjamin[73] pointed to diminished self-consciousness, less worry over sin or guilt, and fewer hypochondriacal ideas. The mood was stabilized, with more self-assertion possible and greater self-esteem. Stevenson and Geoghegan[75] found the operation specific for stabilizing patients with recurrent de-

pressive swings. The following undesirable symptoms disappeared in at least 75 per cent of the cases studied by Freeman and Watts[4]: suicidal attempts, refusal of food, depression, anxiety, hypochondriasis, combativeness, destructiveness, impulsivity and overactivity. Reiner and Sands[154] reported an attenuation of extrapunitive reactions and a decrease in overtalkativeness; Johnson and Benjamin[73] reported that patients were more loquacious, without pressure of speech or flight of ideas. Carscallen et al.[55] noted marked reduction in hallucinations and delusions immediately after operation, but with a tendency to return in three to six months.

Further positive features of personality changes after psychosurgery include the oft-emphasized increased attention to the immediate environment, with less attention to inner thought, less self-concern, obsessive preoccupation and greater readiness to respond to external stimuli. This is also reflected in the greater ability to co-operate with and respond to others. Patients appear more alert and agreeable and enjoy easy laughter. They are more flexible (Jenkins and Holsopple[155]), extroverted, realistic, simple and direct.

On the negative side, may be listed a reduction in depth of feeling, in sensitivity, in complexity of personality and in richness of inner life. Along with a general shallowing of affect, joy is less profound, and awareness of self and others is often superficial. Although happier and better adjusted, the patients react in a less complex, less differentiated fashion. They are honest, complain little, endure hardships and disappointments with equanimity, but lack the drive for leadership, strong sympathies and altruistic involvements. Because of superficial relations, they are poorer at meaningful associations and apparently are unable to take therapeutic advantage of psychoanalytic transference. Rylander's[62] statement that "the soul appears to be destroyed" has been overemphasized to the exclusion of real gains made by many patients. Doubtless, he was referring to the reduction in extent and complexity of feeling, in conflict, in sensitivity to others and in concern with moral scruples that Jenkins and Holsopple described. However, this trend has not been carried to the point of amorality or antisocial tendencies. Carothers[156] finds a similarity between the personality of the lobotomized European and that of the native African. In both, there is a relative idleness of the frontal lobes; there is a failure to see an event as an element in a total situation with a variety of relevant relations.

A brilliant and absorbing account of personality traits after leukotomy may be obtained from the follow-up study of 300 cases by the London psychiatrist, Partridge.[157]

Relief of Pain

Scarff et al.[158-162] have continued to investigate the possibilities of unilateral lobotomy for pain. A five-month follow-up study of 58 unilateral operations for pain, two thirds of them for carcinoma, revealed good results in 38 and fair results in 12. Eight patients had no relief of pain; 7 of these had advanced carcinoma, with impingement of the tumor directly on large nerves. Scarff states that a "unilateral [operation] is permanently effective for pain of constant severity." Pain was relieved, regardless of whether it was on the side ipsilateral or contralateral to the operation, and the operation facilitated termination of severe addiction to narcotics previously used to control pain.

In a study devoted particularly to appraisal of personality changes after unilateral lobotomy for pain, Scarff[161] found no lessening of physical or moral stamina, no weakening of the will to carry on, no disintegration of the personality and no violation of social, ethical or religious code. Sex drive was the same, and affection between husband and wife was not changed. Scarff believed that his patients met the stresses of life as effectively as if they had had two frontal lobes.

King et al.[160] reported on unilateral operation in 6 cases for intractable pain, using the Hardy-Wolff apparatus to study changes in threshold. Of 6 cases, 5 obtained relief from pain; of these 5, the threshold to pain was lowered bilaterally in 4. In the case (a neurotic patient) with no relief of pain, a bilateral increase in pain threshold followed the operation.

Using bilateral lobotomy in 20 cases, Smolik[163] found definite relaxation, indifference and apathy as personality accompaniments of relief. Krayenbuhl and Stoll,[164] from experience in 9 cases, believed that the psychic condition was altered unfavorably if pain was eliminated, whereas if pain was not eliminated, the personality was not affected. They regard the operation as contraindicated in cases of severe pain not due to cancer.

Watts and Murphy[165] believed that a unilateral or an orbital operation may be satisfactory in cases of pain but that a transorbital operation is disappointing, particularly in pain of long standing.

Rehabilitation

Although psychosurgery is a valuable means of treating carefully chosen patients, the operation itself is merely a beginning.[166] Nurses, hospital and community rehabilitative resources, as well as the family, must co-operate if the full improvement potential of each patient is to be realized. Aldrich[167] advises a conservative approach in selection of patients for surgery because of the magnitude of the problems of social adjustment. Greater attention should be given to the attitudes and resources of the patient's family and their feelings toward the patient, and the possible aftereffects of operation should be carefully explained to them. A considerable amount of pre-discharge education and post-discharge supervision should be offered by the hospital.

Active rehabilitation programs have been advocated by Burlingame[168] and by Rackow and McGriff.[169] Burlingame's patients, in groups of 30 to 40, are under constant guidance and drill in personal hygiene. His program includes vocational and avocational training, active psychotherapy and a system of graded privileges.

Rackow and McGriff reported an active physical-exercise program starting on the fourth postoperative day. Exercises on the mats involving bodily contact, bicycle and punching bag workouts, long walks on the grounds, and games and occupational therapy are part of a vigorous program of rehabilitation. Of 37 patients operated on, 27 were able to leave the hospital — a striking record, which speaks volumes for these rehabilitation methods.

Complications

The incidence of postoperative epilepsy varies greatly from series to series. Carscallen[170] and Stevenson and McCausland[171] recently reported over 80 cases with only one postoperative convulsive complication. Many of the factors determining postoperative seizures are apparently unknown, but it appears that older age, preoperative brain damage, extensive surgical procedure, — especially the type involving extensive cortical damage, — posterior sections, postoperative complications, such as meningitis, and more than one operation tend to raise the incidence of seizures. It goes without saying that longer and more careful follow-up study always tends to raise the reported incidence of seizures, particularly if "fainting spells" and atypical attacks are included in the statistics. Rarely do postoperative seizures present a serious problem, for all authors report good response to antiepileptic medication.

Concerning edema of the lower extremities, stiff neck and reluctance to engage in physical activity, sometimes seen in cases after operation, Parsons[172] offers the interesting explanation that this may be due to the use of contrast mediums. Fixation of the medium in the caudal and along the peripheral nerves may predispose to tenderness or pain in the trunk and lower extremities.

For some time, the question has been raised whether lobotomy predisposes the patient to alcoholism, perhaps by a lowering of ethical or moral standards. Talbot et al.[80] have found little tendency to alcoholism. In some of their cases, an opposite trend to relief of alcoholism was noted. These patients had presumably sought refuge in drinking because of neurotic tensions, which the operation allayed, along with excessive indulgence.

Discussion

A previous Medical Progress report[173] should be consulted for developments in the field from the beginning of the modern period of therapeutic frontal-lobe surgery until 1948. The present report covers the pertinent literature of essentially clinical interest since that time.

The introduction of psychosurgery has stimulated interest in brain anatomy and pathology. The connection of thalamic nuclei with the rest of the brain has been carefully traced. Correlation between frontal-lobe sections and clinical outcome has stressed the value of large frontal cuts, sufficient to produce gross personality changes, to obtain therapeutic changes. Pathological evidence favors the idea that amount rather than location of section determines the ultimate result. Extensive neuropathological changes should be expected after lobotomy, with effects felt at a distance from the surgical site, and possibly continuing for a longer time than previously supposed.

Physiologic experiments on lower primates have been stimulated by questions arising in clinical observation of lobotomized patients. The experiments have yielded data on the problem of weight gain, changes in social-status behavior and the differences in function between the medial and lateral halves of the frontal lobes. Physiologic studies in human beings have included investigation of gastric and thyroid function, temperature regulation, cardiovascular dynamics and enzyme activity of the frontal cortex.

Electroencephalographic studies emphasize the potent dysrhythmogenic effect of brain cutting and the positive correlation between dysrhythmia and convulsive postoperative complications, but otherwise there is no relation between the electroencephalogram before or after operation and the clinical outcome.

Psychologic test batteries have been considerably extended since 1948. Evidences of intellectual loss have been creeping in to disturb an otherwise consistent picture of "no change" (prior to 1948). Planning, or rather maze performance, is frequently impaired, but often only temporarily; abstraction capacity and sensitivity are reduced, and responsiveness to outer stimuli is increased. Some "objective" psychologic tests of creative ability have failed to show a loss in this sphere, a finding that goes very much against clinical observation.

Summary

In general, frontal-lobe surgery continues to be recommended for chronic mentally ill patients with very poor prognosis, or for intractable pain. Youth, a well balanced prepsychotic personality, a cooperative family, short duration of illness, a previous tendency to remission and mesomorphic body build have been stressed as favorable prognostic signs. Of especial interest are the experiments in which procaine is introduced into frontal white matter to produce temporary physiologic block, with the object of predicting thereby outcome with more radical and permanent leukotomy.

The results of many hundreds of similar operations are typical of those previously reported — that is, favorable in general, but leaving much to be desired. The improvement (after standard operation) tends to be maintained for years. A variety of types of operation are being studied, and several new ones have been introduced. Work has been done on transorbital lobotomy, topectomy, cortical undercutting, thalamotomy, unilateral lobotomy and medial lobotomy. Almost all modifications of the standard procedure have been advanced by their originators as superior in one or more respects to it; yet it is surprising how few serious attempts have been made to compare several different operations in anything like a critical experiment. For all modifications, long and careful follow-up study is necessary to determine whether or not limited surgery produces lasting results.

Personality changes in patients operated on include both positive and negative features. On the positive side is enormous reduction of tension, fear, worry, combativeness, obsessiveness and so forth, with a turning of attention outward and less preoccupation with morbid inner trends. On the negative side may be listed reduction of depth and complexity of feeling, as well as drive for leadership, strong sympathies and altruistic involvements.

The dramatic reduction of suffering from intractable pain and the elimination of necessity for narcotics have been further explored. Relief may be obtained by unilateral, bilateral or orbital operation but not, apparently, by the transorbital procedure.

Convulsive seizures continue to be the chief complication of frontal lobotomy. However, response to antiepileptic medication is still reported as good, and seizures do not interfere with improvement from psychosis. A tendency to alcoholic indulgence may follow operation in some patients who were preoperative abstainers; on the other hand, several former chronic alcoholics gained relief from their alcoholism after lobotomy.

Psychosurgery has enormously augmented the hope that the relations of brain, intelligence, emotion and personality may some day be made an exact science.

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MEDICAL INTELLIGENCE

CERVICOFACIAL ACTINOMYCOSIS*
Report of Case

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IN the following fairly typical case of cervicofacial actinomycosis, unrecognized for almost five years, a question of the value of various diagnostic and therapeutic methods arises.

Case Report

In September, 1944, a 30-year-old veteran experienced pain and swelling in the area of the right lower wisdom tooth. After ambulatory treatment for "recurrent attacks of pericoronitis" the patient was hospitalized from November, 1944, to February, 1945, and also from March to May, 1945, on account of supervening "submaxillary and cervical lymphadenitis." Discharged from the hospital as "improved," he was under ambulatory medical care until 1949.

According to the hospital records no abnormalities were revealed by diagnostic procedures including physical examination, 4 blood counts, 3 urine tests, a determination of the sedimentation rate, 2 Kahn and 4 heterophil-antibody tests and roentgenograms of the jaw, chest and cervical spine.

During the hospital course 3 cultural attempts for fungous growth, in addition to 2 microscopical examinations for fungi, were negative. In a culture and smear Plaut-Vincent organisms could not be demonstrated. A 5th cultural investigation, whose purpose was not specified, remained without results. In 1946 another culture (object not stated) and in 1949 a 7th attempt to grow pyogenic organisms and tubercle bacilli were unsuccessful.

The records listed the following tentative diagnoses: abscess of the masseter space, with suppurative lymphadenitis; possible fungous, bacterial infection, or tuberculosis; and tissue abscesses of undetermined cause.

The therapeutic measures consisted in repeated incisions of the affected gum area and neck lesions, and in extraction of an impacted right lower wisdom tooth and 3 upper incisor teeth that exhibited chronic periapical abscesses. In addition to the application of hot packs and 4 x-ray treatments "for cervical adenitis" the patient received orally 132 gm. of sulfonamides in 2 courses during November and December, 1944. A total of 3,200,000 units of penicillin was administered by injections of 15,000 or 20,000 units each at 3-hour intervals during January and May, 1945. In 1946 the neck lesions were at one time directly injected with an unrevealed dose of penicillin.

In June, 1949, the patient was examined in my office.

According to his statement the neck lesions had in the preceding years repeatedly assumed boil-like appearance and had discharged pus.

Physical examination revealed adherent scars around the mandibula and a chain of deep-red nodules, most of which were located at the anterior border of the cleidomastoid muscle (Fig. 1). In the discharge exuding from draining lesions sulfur granules were found macroscopically and microscopically. Bacteria were not demonstrable. The smears prepared with Wright's stain exhibited a variegated picture of various white cells, many epithelioid, a number of giant and a few plasma cells.

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To verify the diagnosis 2 culture growths were attempted at intervals of 1 month. The results were negative. A third specimen was simultaneously sent to another laboratory,

FIGURE 1. *Appearance of the Lesions before Final Treatment (June, 1949).*

which reported the following findings: "A microphilic, gram-positive, branched, filamentous organism isolated from granules (*Actinomyces bovis*)."

DISCUSSION

Difficulties encountered in culturing the pathogenic actinomyces, which have been pointed out by most observers,[1-6] must be attributed to several factors. The character of the inoculum, depending on the temporary physical and immunobiologic properties of the originating granulomatous tissue, determines the distribution, paucity or absence of the pathogen in the discharge. Cultural procedures dealing with this type of fungous organism require special mediums and laboratory technics. The prevention of contamination with secondary invaders constitutes another problem. Yet, under rigid laboratory measures, even if subculturing is started with pure actinomyces growth, complete success can hardly be obtained.* Therefore, if discharge material is used for inoculation, negative cultural findings by no means exclude the existence of actinomycosis.

In the search for suspected actinomycotic organisms the direct microscopical examination, routinely employed in laboratory procedures, deserves first consideration. The demonstration of the characteristic ray-fungus colony, macroscopically appearing as "sulfur granules," is practically evidence of actinomycosis, since only in rarer diseases are such forms found.[8] The absence of these granules may be explained by the prevailing condition of the discharging tissue, or it may indicate the presence of aerobic pathogenic actinomycotic organisms that do not produce such structures.[9]

The direct examination of the smear revealing microbial and cytologic content may give valuable information in the differential diagnosis of pyogenic granuloma, tuberculosis, syphilis, neoplasm and so forth.

In addition to the use of smear and culture, agglutination,[2, 3] complement fixation and skin tests[3, 8] have been tried and yet have not found general acceptance. Inoculation of laboratory animals is reported to be successful in about 50 per cent of cases.[2, 6] In biopsy the diagnostic criterion rests on the demonstration of the micro-organisms, not on the appearance of the unspecific granulomatous tissue changes. Results with this method[10] did not favor its use as a routine diagnostic measure, especially since it is not always applicable.

The advent of the sulfonamides and antibiotics has greatly improved the chances for a cure in actinomycosis. In their selection one should consider their effect on secondary invaders. Under such circumstances, a combination of various remedies may prove valuable. Differences in sensitivity of various strains to a particular remedy[8] may be disclosed by sensitivity tests in vitro. To obtain effective dosage the determination of the tissue concentration might be helpful.

Nevertheless, mechanical conditions, such as bone involvement, accumulated pus and dense granulomatous tissue, are likely to produce foci inaccessible to the therapeutic agent. In cases of this kind an operation is indicated.[8] Iodine preparations as well as x-rays, which act on the diseased tissue, can also be expected to retain their place as time-tested adjuncts.

SUMMARY AND CONCLUSIONS

A report of a case of cervicofacial actinomycosis, not recognized for about five years, is presented.

Difficulties frequently encountered in establishing the diagnosis of actinomycosis are discussed.

Among diagnostic methods the examination of the smear deserves first consideration. The direct study of the cytologic and microbial picture is also helpful in differential diagnosis.

*In Dobson's "15-control" tests in which *A. bovis* was grown in thioglycollate only 80 per cent were found to be positive.[6] Lamb et al.[3] point out: "Not until the third or fourth subculture could we obtain growth on any medium save that first mentioned." Lewis[7] expresses his view in this respect as follows: "The difficulty of carrying out cultural studies precludes this manner of study from universal use."

Penicillin proved effective in achieving a final cure. During an observation period of three years no relapse has occurred.

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THE RELATION OF HEART SIZE TO THE TIME INTERVALS OF THE HEART BEAT, WITH PARTICULAR REFERENCE TO THE ELEPHANT AND THE WHALE

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BOSTON AND SEATTLE

ONE of the moot questions in human electrocardiography is that of the normal upper limit of the atrioventricular conduction time (PR interval) and of the duration of the spread of the excitation wave through the ventricles (QRS complex). It is the general consensus that the former may measure from 0.10 second or even a little less in the healthy newborn infant to 0.20 second or even a little more in the healthy full-grown adult, and that the latter may measure from about 0.05 second in the infant to about 0.10 second in the adult. The change from the shorter measurements to the longer takes place gradually with the growth of the heart. It is not, however, adequately appreciated by all concerned that larger adults with larger normal hearts or that persons of any age with enlarged hearts due to strain from hypertension, systemic or pulmonary, or from valvular disease may have electrocardiographic time intervals a little above the generally recognized upper limits of 0.20 second for PR interval and 0.10 second for QRS duration without having myocardial disease per se to produce either atrioventricular or bundle-branch block. Thus, on occasion, persons with apparently normal or with simply enlarged hearts may have PR intervals measuring up to 0.21 or even 0.22 second or QRS complexes measuring up to 0.11 or even 0.12 second.

In 1916 White and Kerr[1] dissected the heart of a young sperm whale and found a clearly differentiated and extensive atrioventricular conduction tract with large Purkinje cells; this heart was 56 cm. broad and 33 cm. long. The atrioventricular bundle was 1 cm. wide. Soon after that, Burwell and White (1920) dissected the heart of a forty-year-old elephant (Mollie) and again found an extensive conduction system, which was confirmed later by King in the case of the elephant Tusko, which was forty-three years old. King, Burwell and White[2] reported on the anatomy of these 2 elephant hearts in 1938.

A companion article in the same number of the *American Heart Journal* in 1938, written by White,

FIGURE 1. *Jeff Davis, Expert Whale Hunter, with Harpoon, Showing Electrode Head with Insulated Cable and Nylon Cord.*

Jenks and Benedict,[3] concerned the electrocardiograms of 9 healthy circus elephants (Juno, Modoc, Tillie, Myrtle, Lizzie, Clara, Queen, Pigmy and one whose name is not remembered). These observers found that the heart rate of the elephants averaged about 35 per minute (range from 24 to 53) and that the PR interval and QRS duration were about twice those of the normal human adult — that is, 0.28 to 0.41 second and 0.12 to 0.18 second respectively. Since the newborn human infant has about twice the heart rate and half the PR interval and QRS duration of the normal human adult, and since a small mammal such as the mouse§ has corresponding differences in heart rate and time intervals as compared to the human infant, it was suggested in 1939 that there might be similarly considerable differences between the heart rates

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†President, American Heart Association.

‡President, Heart Council in Cambridge.

§The electrocardiograms of 4 mice showed heart rates varying from 620 to 780 per minute, PR intervals varying from 0.03 to 0.04 second and QRS durations ranging from 0.008 to 0.011 second (information obtained from M. Rappaport, of the Sanborn Company, Cambridge, Massachusetts).

and time intervals of the elephant and those of a large whale, which, of course, has a much larger heart.

In 1940 we proposed to obtain an electrocardiogram of a whale with the help of Governor Gruening of Alaska and the United States Bureau of Fisheries, but World War II intervened and we all became greatly preoccupied.

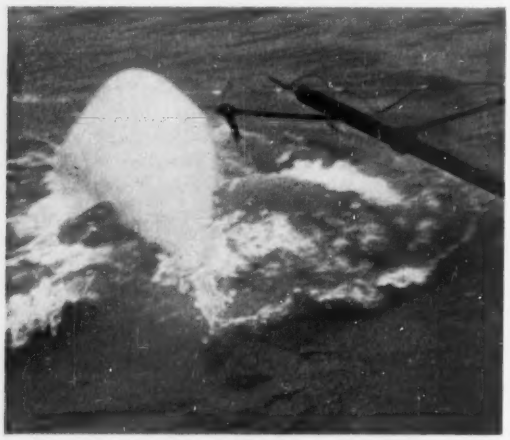

FIGURE 2. *"Moby Dick, Jr.," Towing the Skiff Used As a Whale Boat, Showing Two Connections Already Established. The large holding rope had been inserted by the first harpoon shaft, which is still visible, tipped by a point that fitted into the harpoon head. The nylon cord and insulated cable (looped and attached to the cord) are inserted into the second harpoon shaft, which is not visible.*

During the past year, however, plans went forward again, and with the generous help of the Alaska Packers and in particular Mr. Delebecque, of King Salmon, Mr. Don Cooper at Clark's Point and several of his staff, in particular Jeff Davis (Fig. 1), skillful hand harpooner and Joe Clark, able skipper, we succeeded, after several vicissitudes, in early August in obtaining by the use of bipolar harpoon electrodes a dorsal electrocardiogram of a Beluga whale (Fig. 2). This small species was selected because it was readily available, could easily be reached and was small enough to permit us to develop our technic, which we hope to be able to apply to a large whale at some later date.

Details of this experience and our findings will be published elsewhere, but the present note seemed advisable to establish the scientific background for this exploit. Suffice it to say herewith that the record made while the whale was pulling us along in our 20-foot skiff showed a heart rate varying from 12 to 23, with an average of 15 to 16, indistinct inverted P waves with PR intervals of about 0.3 second, diphasic QRS waves of low amplitude and inverted T waves. The heart of the Beluga whale, the record of which we obtained, was actually not so large as that of Mollie, the elephant, or as the heart of the young sperm whale that was dissected in 1917. It seems quite clear that an important factor in reducing the heart rate to this low figure was that of the vagal effect of diving and immersion, as Irving, Scholander, and Grinnell[4] have already pointed out in a study on the seal.

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MASSACHUSETTS PHYSICIANS ART SOCIETY

11. My Debbie

Exhibited at American Medical Association, San Francisco, 1950

Award of Merit Sculpture in Carrara Marble

by

NATHAN L. FINEBERG, M.D.

Associate Professor of Otolaryngology
Boston University School of Medicine

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

BENJAMIN CASTLEMAN, M.D., *Editor*

VIRGINIA W. TOWNE, *Assistant Editor*

CASE 39021

PRESENTATION OF CASE

A twenty-eight-year-old woman entered the hospital because of a cough.

Two weeks before admission the patient, who had been active and apparently well, developed a "head cold," and began to have a painless, hacking, mildly irritating cough, productive of small amounts of whitish, nonbloody sputum. Two days later she began to feel ill and vomited three or four times. She became tired, listless and quite drowsy, and experienced drenching night sweats, with a temperature rise to 100 to 101°F. each evening. Her physician found nothing abnormal on physical examination and prescribed cough medicine and later aureomycin, 1 tablet every four hours for 18 doses. Despite this medication the patient stayed in bed, since she continued to feel feverish, tired, sweaty and anorectic. There had been a slight increase in the hacking cough, which was now productive of half a cupful of white phlegm each day. Three days before entry the temperature fell to normal, and the patient felt somewhat better. A roentgenogram of the chest taken at this time was reported as showing a mediastinal mass. Cough, sputum and malaise persisted and the patient entered the hospital.

The patient had never had any previous illnesses similar to the present one. There was no history of previous cough, fever, sputum, hemoptysis or chest pain. As far as she knew she had no recent exposure to tuberculosis. There was a questionable weight loss of 10 pounds; otherwise, the systemic review was essentially negative.

Physical examination revealed a young woman in no distress, except for occasional paroxysms of hacking, nonproductive cough. There were a few small lymph nodes palpable in the right supraclavicular fossa. The lungs and heart were normal; there was no increase in mediastinal wideness. There was no clubbing of the fingers, and the remainder of the examination was negative.

The temperature was 98.6°F., the pulse 90, and the respirations 25. The blood pressure was 110 systolic, 70 diastolic.

The urine was normal. Examination of the blood showed a hemoglobin of 10.5 gm. and a white-cell count of 10,600, with 77 per cent neutrophils, 14 per cent lymphocytes, 2 per cent monocytes, 5 per cent eosinophils and 2 per cent young neutrophils. A smear of the blood revealed a + variation in the size of the red cells. The prothrombin time was 16 seconds (normal, 13 seconds). A stool was guaiac negative, and a cytologic examination of the sputum was reported as "doubtful" for malignant cells. Fluoroscopic examination of the chest disclosed an irregular, slightly nodular, soft-tissue mass in the anterosuperior mediastinum that displaced the aortic arch downward and the trachea slightly posteriorly. The mass did not move on swallowing and showed no change in size on Valsalva or Müller maneuver. The vocal cords moved freely. There were a few strands of increased density on the anterior surface of the right upper lobe. A small amount of fluid was present in both costophrenic sinuses; diaphragmatic motion was free and equal. There was no significant lymph-node enlargement in the paratracheal, intrapulmonary or posterior mediastinal groups (Fig. 1 and 2).

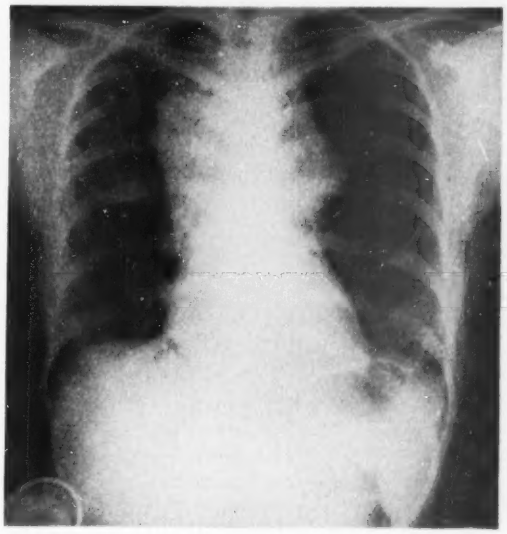

FIGURE 1.

In the hospital there was little apparent change in the patient's condition. On the sixth hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. HELEN S. PITTMAN*: "The mass. . .showed no change in size on the Valsalva or Müller ma-

*Associate physician, Massachusetts General Hospital.

neuver." Does everyone except me know what the Müller's maneuver is? I did not know and had to look it up. It is just the opposite of the Valsalva maneuver: the patient expires fully, closes the glottis and attempts to inspire; whereas in the Valsalva maneuver, the patient inspires, closes the glottis and attempts to expire. Is that right, Dr. Wyman?

DR. STANLEY M. WYMAN: Yes; in the Valsalva maneuver the intrathoracic pressure is increased, whereas in the Müller procedure it is decreased.

DR. PITTMAN: In the Valsalva maneuver intrathoracic pressure is increased, and the heart becomes

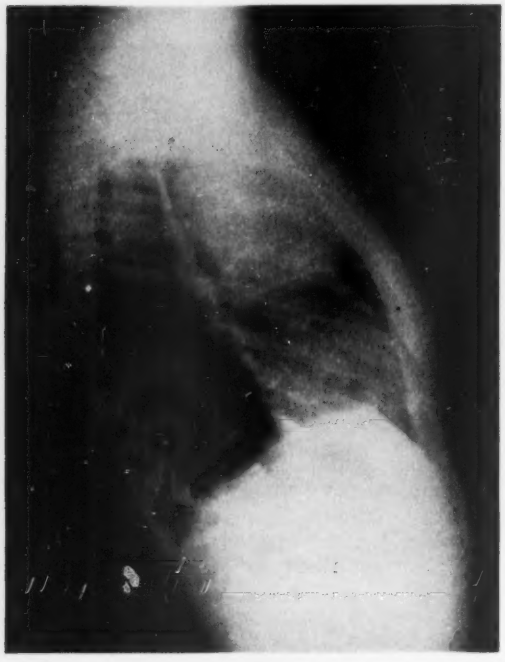

FIGURE 2.

smaller; in the Müller maneuver the opposite takes place. It becomes important if one is considering a mediastinal cystic mass; one can, I am told, fairly well put his money on its changing size during these maneuvers.

This history boils down, I think, to a process in the mediastinum that had to do with infection — either induced or aggravated by infection. Concomitant findings were a few supraclavicular lymph nodes, a small amount of fluid in both pleural cavities, a slight change in white-cell count and slight elevation of the prothrombin time. This was a healthy woman. I think there are enough women of twenty-eight who have a hemoglobin of 10.5 gm. and some variation in size of red cells so that I am not going to attribute much to that. I am not going to pay any attention to the tuberculosis because I do not think that has anything to do with the picture.

There was a note in the protocol only of fluoroscopy; are there any films?

DR. WYMAN: This large, somewhat irregularly outlined mass lies in the upper mediastinum far anteriorly (Fig. 1). The trachea is displaced posteriorly and is somewhat compressed, as you can see in the oblique film (Fig. 2). The changes in the upper lobe are those of atelectasis, with perhaps some pneumonitis in the anterior segment of the right upper lobe. As far as one can tell, the hilar shadows are not unusual, but they are so obscured by the mass that I do not think I can be certain. There is no evidence of bone destruction. The bronchi show no intrinsic changes, although they are somewhat narrowed. There is some fluid in the pleural spaces.

DR. PITTMAN: The reason that led me to medicine rather than surgery was that as a student I thought that surgery consisted of the differential diagnosis of lumps, which I thought was a very dull field. I shall include in this discussion as little dullness as possible, although it boils down to a differential diagnosis of a lump. One never knows what a lump is until he has his hands on it or a piece of it under the microscope or both. This lump was in the anterior superior mediastinum. I am going to talk about what seems to me to occur in the superior mediastinum. The first is mediastinitis or mediastinal abscess. We have nothing to make a logical case for mediastinal abscess. This woman had a respiratory infection, to be sure, but in most cases of mediastinitis there has been either surgery on the neck or trauma, so there is no reasonable background for making a diagnosis of mediastinitis or mediastinal abscess. Therefore, since I think infection is what precipitated this episode, I am going to talk about infection in structures within the superior mediastinum. There may have been an intrathoracic thyroid gland. It usually moves with swallowing; is that right, Dr. Wyman?

DR. WYMAN: Yes; sometimes when an intrathoracic thyroid gland is very large, it is trapped behind bony structures, but usually it moves on swallowing.

DR. PITTMAN: I cannot find any cases in which a thyroglossal-duct cyst presented so low, and I am going to throw that possibility out. That leaves me with the great vessels and trachea. First of all, I do not think there is any reason to assume that the mass was vascular. Cysts may arise from the trachea and from the esophagus. They are not common, and they would probably change in position on these maneuvers with changes in intrathoracic pressure. A previously existing cyst communicating with either the trachea or the esophagus would satisfy a good many criteria. Something happened to this patient after she got an ordinary

cold. She began raising a good deal of sputum, I gather, not too long before she began to feel better; suggesting that when she began to produce half a cupful of white phlegm each day she was decompressing something and that the decompression had a causal relation to the temperature's falling to normal and her beginning to feel better.

It seems to me a more logical diagnosis for this lesion is that it was a mass of thymic origin. Then I can assume that it was a simple cyst or a more solid structure of teratoid nature — using that term to cover both dermoid cyst and teratoma. There are radiologists who believe that teratomas of the thymus may be suspected when a lobulated mass is present. That may be going out on a limb, but it is a very convenient limb so I am going to pick on it at the moment.

What caused the fluid in the pleural cavity? I am inclined to think, now that I have seen the films, that there was probably enough pressure to produce a simple mechanical fluid. There is a detailed article,[1] which I have read only in abstract, on the anatomy of the mediastinum and its drainage, describing the role of the phagocytic cells that block dissemination of irritants from the pleural cavities to the mediastinum and move particles introduced into the mediastinum away from the midline toward the pleura. I shall assume that the fluid was secondary, mainly mechanical from pressure.

I shall settle for a diagnosis of a tumor of the thymus. These tumors are usually silent for a long time and make themselves known in late adult or early middle life. I think there was secondary infection from the upper respiratory tract. How it got there is a little tenuous. Somewhere, there was a bronchial communication to account for the sputum. I believe the patient had a teratoid, essentially silent, tumor of the thymus, either dermoid or teratoma, and secondary infection.

Dr. Alfred Kranes: A year and a half before admission the patient had x-ray films of the shoulder, which showed the mass to be present then.

Dr. Pittman: That delights me.

Dr. Chester M. Jones: If there is compression of the trachea, would not more or less infection be bound to occur behind it?

Dr. Pittman: It seems to me that there is always enough going on there so that it would.

Dr. Bernard M. Jacobson: On a statistical basis, Dr. Pittman, would not lymphoma rather than thymoma or colloid goiter be more likely?

Dr. Pittman: I believe statistically that they are the most common tumors in that region. I forgot to discuss the tumors of lymphoid tissue while I was standing on my feet. I had thought about them, since they are the most common tumor in that location. I was riding a limb that appealed to me and I did not look at my notes. I suppose that, statistically, a thymic tumor would come last. I am somewhat prejudiced by the fact that I had a case of teratoma of the thymus within the year.

Dr. Benjamin Castleman: Although Schlumberger[2] believes that all mediastinal teratomas and dermoid cysts arise from the thymus gland most pathologists think that they arise not from the thymus gland but from an embryologic remnant of one of the branchial clefts in the anterior mediastinum. We think of a thymic tumor as arising from the two types of cells within the thymus and designate it as a thymoma. The dermoid cysts and teratomas are tumors of the anterior mediastinum. What you meant was an anterior mediastinal tumor, not necessarily a tumor arising from the thymus gland?

Dr. Pittman: As I understand it, the thymus gland and the structures that give rise to teratomas are derived from the branchial clefts, usually the third or perhaps the fourth, which all come wandering down together. The thymus wanders down routinely and usually atrophies; the teratomas come in only occasionally, but they all derive from a common ancestor in that they all come from the same embryologic part of the body.

Dr. Castleman: Yes; that is true, but I think it is clearer to most people to separate the dermoid cyst and teratoma in the anterior mediastinum from the thymoma, which gives a different prognosis and which is a different tumor.

Dr. Pittman: I shall accept that; I was not talking about a thymoma.

Dr. Kranes: Fortunately, we were not pinned down as Dr. Pittman was, and our diagnoses varied. My own opinion was that this was either a teratoma or a thymoma, but it was quite apparent that the only way the diagnosis could be made was by examination of tissue. A difference of opinion arose regarding where to begin. Dr. W. Allan Tisdale, who admitted the patient, suggested that we biopsy one of the two small supraclavicular lymph nodes that he had found. They seemed to be so unimpressive that I believed the only way we could be sure of a correct diagnosis was to biopsy the large mass. That was done by Dr. Richard H. Sweet, who found a large infiltrating mass, which he was unable to remove, so he took a small piece for biopsy. It was his impression at the time of operation that it was a malignant thymoma.

Clinical Diagnosis

?Teratoma, ?malignant thymoma of mediastinum.

Dr. Helen S. Pittman's Diagnosis

Teratoma of mediastinum.

Anatomical Diagnosis

Malignant lymphoma, Hodgkin's type, of anterior mediastinum.

Pathological Discussion

Dr. Castleman: Since Dr. Sweet is not here, I shall read an excerpt from his operative note:

> The growth was rather adherent on the right side to the undersurface of the sternum and costal cartilages. There was a large, nodular, irregular, firm tumor bulging into both pleural cavities. There was considerable fixation to the underlying tissues, including the innominate vein, the vena cava and the great arteries going to the head and neck.

The tumor was, therefore, large and infiltrating; the biopsy showed characteristic Hodgkin's disease.

There have been a few papers within recent years describing tumors of the anterior mediastinum believed to be thymomas that have large multinucleated cells said to be indistinguishable from the Reed-Sternberg cells of Hodgkin's disease. I strongly believe they are not thymomas but the ordinary type of Hodgkin's disease, because many of those patients have gone on to develop lesions in other parts of the body just as patients with Hodgkin's disease do. Metastasis of a thymoma outside the chest rarely, if ever, occurs. In the case under discussion I do not believe that even adherents to the idea of a peculiar type of thymoma with the Reed-Sternberg type of cell would call this a thymoma because, in addition to the multinucleated cells, there were fibrosis, eosinophils and the immature lymphocytes seen in Hodgkin's disease.

After the operation the patient received x-ray treatment to the mediastinum.

Dr. Pittman: This again brings up the point that I made at the beginning about these lumps, the nature of which remains unknown until they are examined under the microscope.

Dr. Jacobson: I do not think that is always true. If one can find a peripheral lymph node and take it out, one can make the diagnosis.

Dr. Castleman: Our experience has shown that these small cervical lymph nodes that are barely palpable prove to be inadequate for diagnosis so that one eventually has to biopsy the main mass. That is undoubtedly why Dr. Kranes chose not to have a biopsy of the lymph node.

In some hospitals this patient would have received at least a therapeutic x-ray dose without any biopsy. In this hospital, the radiologists refuse, and rightly so, to give x-ray treatment to a mediastinal mass until they know what it is. We have had a patient with a mediastinal mass that was treated by x-ray and was later found to be tuberculous, with death due to miliary spread.

Do you have any films showing the mass after treatment?

Dr. Wyman: The patient had a large tumor dosage of nearly 3000 r since we expected to stop the disease and there was only one proved site. These two films, taken after x-ray therapy almost two and a half months after the original examination, show a definite decrease in size of the mass (Fig. 3).

Dr. Jacobson: It is a pity that this tumor was not operated on a year and a half previously. About five years ago I saw a young woman of about the same age, with a similar history, a similar-sized mass and also with a diagnosis of Hodgkin's disease microscopically. Dr. Sweet was able to remove the entire tumor. Thereafter she had x-ray therapy.

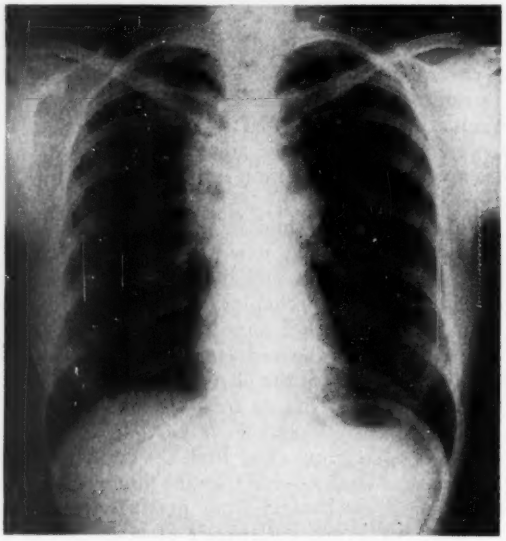

Figure 3.

She is still living and well without any recurrences after five years.

Dr. Jacob Lerman: Do you think you should consider surgery now after x-ray therapy?

Dr. Castleman: I doubt if it could be removed now. The pulmonary symptoms are no longer present. This patient re-entered the hospital about three months later and had a hysterectomy for a large fibroid.

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CASE 39022

Presentation of Case

A thirty-one-year-old man was brought to the Emergency Ward by police ambulance because of chest pain.

For the past several years, the patient had had frequent episodes of sharp chest pain, usually starting on the left side and radiating to the right and accentuated by deep breathing. The pain lasted for a few minutes to hours, and had occurred almost

weekly during the early part of the previous year. A roentgenogram of the chest was taken about six months before entry, but the patient received no report about it. The present pain began about ten days before admission and apparently did not differ from previous episodes. It was most severe behind the sternum, was said to be aggravated by deep breathing or coughing, was present all the time and became especially severe on the day of admission. He denied having a cold, chronic cough or hemoptysis. Despite the pain he continued to work up to the day of entry.

Two years before admission, he lost about 35 pounds of weight, and did not work for a whole year. A relative said that he was in a depressive state during that period. He saw several doctors but nothing was done. He slowly regained his weight and energy and desire to work but nevertheless had been idle most of the year before entry. Three years before admission he had an episode of "pleurisy" during which the chest pain was similar to the present one. A sister had been operated on for tuberculosis two years before the patient's admission.

Physical examination revealed a fairly tall, well developed and moderately nourished man complaining of retrosternal pain on deep breathing. There was dullness to flatness over the right anterolateral aspect of the chest, with decreased bronchial breathing. There was tenderness over the sternum and along the fourth to sixth ribs on both sides on percussion. No rales or friction rub was heard. The heart size was normal, and rhythm was regular. A Grade 1 apical systolic murmur was present. The upper abdomen was guarded, but there was no tenderness or mass. The extremities were normal.

The pulse and respirations were normal. The blood pressure was 126 systolic, 80 diastolic.

About an hour after entry, when the patient was being wheeled to the Radiology Department, he began to have labored breathing; the eyes were turned upward; the teeth clenched, and he was rigid, with both hands in hyperextension. For a moment he appeared to be having a convulsion. He was taken back to his room, and oxygen was started immediately after the insertion of an airway. However, the respiration became slower, irregular and spasmodic; the pulse and heart beat were unobtainable, and he died shortly afterward.

Differential Diagnosis

Dr. Edwin O. Wheeler*: The last patient I discussed here lived for three hours; this one lived one hour after entry; I suppose the next one will be dead on arrival.

I should like to ask if the patient's temperature was taken; there is no record of it here. Were the dullness and flatness limited to the anterior part of the chest, or were they also present posteriorly?

Dr. Edgar B. Taft: There is no record that the temperature was taken. The dullness and flatness were present only in the anterolateral portion of the right chest.

*Assistant in medicine, Massachusetts General Hospital.

Dr. Wheeler: There is not a great deal of information in this case because of the patient's sudden death, which in itself is the best lead and most characteristic feature of the illness. I thought it might be well to approach the problem by going over the diseases that might be expected to cause sudden death in a patient of this age. According to the New York City Medical Examiner's office,[1] out of 87 sudden deaths in men of this age 84 per cent were caused by disease of the heart and aorta, respiratory tract or nervous system, and another 9 per cent by malaria in drug addicts, and only 5 deaths by other conditions. I think I might best consider diseases of the first three systems. The past history and illness prior to admission do not suggest neurologic disease; therefore, I shall omit that from consideration.

What about respiratory-tract disease? The leading respiratory causes of sudden or unexpected death in men of this age are pneumonia, tuberculosis and occasionally pneumothorax or hemopneumothorax. The patient's history of symptoms over a period of several years and the absence of respiratory distress, cough, hemoptysis and, I should guess, of fever, as well as the sudden death at the end of the illness, are against the diagnosis of an acute respiratory infection. Tuberculosis needs to be considered more seriously because he had some chronic disease preceding death with a period of weight loss, a history of pleurisy and a positive family history for tuberculosis. Against the diagnosis of pulmonary tuberculosis are the absence of cough and hemoptysis and the fact that he had regained his lost weight, that he appeared in good health at the time of entry and that he died extremely suddenly. Patients may die extremely suddenly from pulmonary tuberculosis with hemorrhage, but the hemorrhage should be obvious at that time.

A pneumothorax or hemopneumothorax occasionally causes sudden death or relatively sudden death in a man of this age. I should not expect a history of several years of pain in this condition. Patients may have repeated episodes of spontaneous pneumothorax, but it seems unlikely that such attacks would cause pain of this frequency. Furthermore, the patient's apparent good condition on entry, without tachycardia and without shortness of breath, is against that diagnosis. Finally, a pneumothorax or hemopneumothorax large enough to endanger the patient's life would scarcely have been overlooked in the Emergency Ward. There are other rare diseases of the respiratory tract, which I shall not consider.

Diseases of the heart and aorta are the most common causes of death in men of this age. They include coronary-artery disease, rheumatic heart disease, massive pulmonary embolism, occasionally acute cardiac tamponade as the result of pericardial effusion and a ruptured aortic aneurysm, either

dissecting or syphilitic. Coronary-artery disease accounts for two thirds of all the sudden deaths in men of this age, and this patient's sudden death was preceded by substernal pain. However, the character of the pain for two or three years preceding this episode does not suggest angina pectoris, and the duration of the pain — ten days — during the acute illness, would be unusual for myocardial infarction. Furthermore, coronary-artery disease would not account for the physical findings in the anterior part of the chest. I should have expected some abnormality of the pulse, respirations, blood pressure or heart sounds. I think a most important clue is the fact that the house staff thought he ought to have chest films before he had an electrocardiogram.

Rheumatic heart disease, I think, is quite unlikely. Massive pulmonary embolism may cause sudden death, but again the chronic nature of the illness, the absence of a source for pulmonary emboli, the absence of dyspnea and tachycardia and the normal blood pressure are perhaps against this diagnosis.

Dissecting aneurysm is a favorite topic at these sessions, and it might occur in a man of this age. Patients have been seen with dissecting aneurysm at the age of thirty-one. However, this is an extremely acute disease, does not last ten days and does not cause symptoms for two or three years. Finally, I should not have expected him to have normal vital signs by the time he came to the hospital if he had a dissecting aneurysm.

Syphilitic aortitis, with involvement of the mouths of the coronary vessels, may produce sudden death. I think I can exclude it by the same means as I excluded coronary-artery disease per se. A syphilitic aneurysm would be unusual in a man of this age, but it can occur. It would account for the symptoms of several years' duration that had been increasing in severity up to the time of admission. The location of pain substernally, aggravated by coughing and breathing, is consistent with an aneurysm of the ascending portion of the aorta. Yet the only symptom was pain, which is unusual. It is also unusual for the pain to be intermittent for several years before death. Most patients complain of other symptoms because of pressure of the aneurysm such as dyspnea, hoarseness and difficulty in swallowing. The only abnormal physical findings at the time of entry were dullness and flatness in the right side of the chest, and parasternal and substernal tenderness, which could be associated with an aneurysm of the ascending aorta. The blood pressure, pulse and cardiac findings may all be normal in this condition, as they were in this case. Finally, rupture of an aortic aneurysm may account for sudden death. The history in this case suggests that perhaps the pulse and heart beat became unobtainable before the respirations disappeared — that could be accounted for by the rupture into the pericardium, which caused almost instantaneous death.

DR. TAFT: This patient was obviously not expected to die, as Dr. Wheeler suspected, when he was sent to the Radiology Department. When he came to us, it was questioned whether he had pneumonitis, myocardial infarction or possibly a pulmonary embolism.

CLINICAL DIAGNOSIS

?Pneumonitis.
?Myocardial infarction.
?Pulmonary infarction.

DR. EDWIN O. WHEELER'S DIAGNOSIS

Syphilitic aneurysm of ascending aorta, with rupture into pericardium.

ANATOMICAL DIAGNOSES

Coronary atherosclerosis, severe, with sudden death.
Pulmonary congestion and edema, severe.
Cerebral edema, severe.
Chronic gastric ulcer.

PATHOLOGICAL DISCUSSION

DR. TAFT: At autopsy the aorta was not remarkable, and there were none of the other findings that Dr. Wheeler suggested as possibilities. The striking findings were the severe pulmonary congestion and edema and the marked coronary atherosclerosis. The lungs weighed over 2000 gm. — at least three times the normal weight. Microscopical examination of the myocardium showed much less than we might have expected after a three-year history of repeated episodes of sharp chest pain. There was little increase in interstitial fibrous tissue. The main change seemed to be in the coronary vessels, which showed the usual type of atherosclerosis throughout, with increase in subintimal fibrous tissue, cholesterol clefts, calcification and some chronic inflammatory cells. This was of interest because it was quite different from the atherosclerosis of youth that Leary[2] described in which the picture is similar to that seen in rabbits fed cholesterol. The atherosclerosis found in this patient was the type that Dr. Leary associates with the ages of forty to sixty. This, then, was a case of death from severe coronary-artery disease, although no definite occlusion was found at autopsy.

There was an incidental chronic gastric ulcer, which was not active although the mucosa was not intact over it. There was no evidence that the patient had bled or anything to suggest that it was associated with his death. An additional finding, which we were unable to explain and which may have had some significance in his death, was a severe cerebral edema. The brain weighed 1590 gm. and showed marked flattening of the convolutions and narrowing of the sulci. The neuropathology laboratory had no suggestions regarding etiology other than that he might have been anoxic for the period just before death.

REFERENCES

1. Rabson, S. M. Sudden and unexpected natural death. V. Causes of death classified by sex and age. *Arch. Int. Med.* **86**:361-375, 1950.
2. Leary, T. Experimental atherosclerosis in rabbit compared with human (coronary) atherosclerosis. *Arch. Path.* **17**:453-492, 1934.

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THE HEALTH NEEDS OF THE NATION

Almost exactly a year ago, in the face of considerable criticism from high quarters and the implication that politics were providing the *vis a tergo* for the presidential establishment of a commission to study the health needs of the nation, this *Journal* nevertheless assumed that reasonably lofty motives were behind the action. The Commission was headed by a surgeon whose integrity and breadth of patriotism are above reproach, and its composition was otherwise representative of various interests and points of view, both conservative and liberal. All its members have worked throughout the allotted year with loyalty and devotion to their task, and often at great personal inconvenience.

A year is too short a time in which to bring forth the answers to many of the questions that are uppermost in the minds of health-conscious persons. Nor would two or three or five years be long enough, for some of these questions can be answered only with knowledge not yet available. Basic concepts of right and wrong, of high principles and of expediency will change, also, and some of that which is anathema today (as were prepayment plans for hospital care twenty years ago) will seem to represent reasonable and intelligent progress tomorrow. One of the most difficult facts to accept is that only through patience can one learn the answers that only time can bring.

The report has already been published, analyzed, commented on, praised and attacked, and at this relatively late date after its release there is no particular point in making other than brief remarks concerning any of its principles or recommendations. Many of these recommendations will surely turn out to be acceptable — some of them after modification; a few will be acknowledged as unsound according to present standards and will eventually be rejected, but there need be no question that all are since e and honest.

The fundamental premise that "access to the means for the attainment and preservation of health is a basic human right" must be accepted rather as a pious aspiration than a cosmic principle, for human rights are only what human beings have declared them to be and may vary, and have varied, from time to time and from place to place and according to the practicability of their attainment.

The report brings more clearly into the open than some of the proponents of some of the existing prepayment plans have been quite able to acknowledge the problem of low-income groups and the necessity for preparing to meet what may reasonably be considered as their basic needs. It may be that all elements of the population neither can achieve nor especially desire health facilities on a par with those of all others. Neither are all fed, clothed or educated alike, although it is cherished as an American ideal (let it be

hoped that it is not merely an American illusion) that eventually all will be given equal opportunities for the attainment of equal rewards commensurate with their own efforts.

The matter of that cherished desideratum of "human dignity" in relation to the provision of medical care is again emphasized. These are very fine words indeed and must be held in respect, even as one recalls that the human dignity of a great many extraordinarily fine people is daily outraged by bus drivers, military personnel, police officers, tax collectors, courts of law and various representatives of officialdom up to and including some of the very highest. The day when the lion, the lamb and the jackal will lie down together in mutual harmony is devoutly to be anticipated; meanwhile the lamb may have to accept a few thoughtless roars with that quiet smile of which only lambs are capable, regardless of their inner feelings.

The Commission favors the prepayment principle to provide "almost complete protection" against the costs of medical care, with the removal of bans against consumer-sponsored plans, the extension of preventive medicine, federal aid to medical education, the expansion of private and governmental support of research, especially in mental disease, a federal department of health and security, and, wisely, further study of many of the problems encountered. It favors a voluntary federal-state program for financial assistance in bringing to the people the advantages that it recommends, which immediately aroused the guardians of free enterprise in medicine, fearful of any revival of national compulsory health insurance.

The mistake that is made in the reception of such a study is to look mainly at the tentative answers and try and pick out the bad ones, as an unhappy diner, concerned only with the bones in a plate of fish, forgets that some excellent meat may also be present and may, indeed, constitute the chief virtue of the dish. The value of this report is not so much in the details of its recommendations as in the very fact of its having been made.

CENTENNIAL OF REFERENCES

A LITTLE over a hundred years ago, on July 8, 1850, Monsieur Chatin, a French chemist, deposited with the secretary of the Académie des Sciences a sealed letter. On August 26 of the same year, he stood before that august body and rendered a report entitled "Researches on the Iodine Content of Fresh Water and the Presence of this Substance in Plants and Terrestrial Animals." Subsequently, on September 30, Chatin asked that the "paquet cacheté" deposited by him on July 8 be opened in public audience — "en séance publique." The letter was found to contain a dated communication announcing that Chatin had just detected iodine in minute but appreciable quantities in rain water as well as in plants. On the other hand, he acknowledged in the same sealed letter that Cantu, of Turin, was the first person who had reported the presence of iodine in potable water and thus possessed the honor of discovery.

A century ago communication in print was distinctly limited, and Chatin's paper of August 26 is not given in full but in a summarized form. Iodine is stated to be present in variable proportion in the waters of the globe in association with iron, especially in rivers that course through igneous formations. On the other hand, it was pointed out that waters of rivers that arise in glaciers, such as the Rhine and the Rhone, are poor in iodine. After presenting the relative iodine values of different foods the author advances the remarkably modern suggestion that the specific prophylaxis of goiter could be accomplished by the substitution of (iodized) salt from a salt marsh for the rock salt habitually used in regions in which goiter is endemic.

In the *Comptes Rendus* of the Académie des Sciences for 1850, the general pattern of publication consists in a presentation of data in summarized form, with few if any facts or, at least, quantitated facts. Usually, no references are given although occasionally a single reference is made to an article published previously in the *Comptes Rendus*. *Paquets cachetés* are common, and sometimes one finds such grudging admissions as that made on page 137: "I should observe that my experiments concerning the action of sodium carbonate on codein were made before I had read the note of M. Wertheim, published in the February issue of the Annals of Chemistry and Pharmacy."

Here are apparent the motley ancestors of the references that today accompany, like a blue-ribbon pedigree, almost every published paper. Gone are the *paquets cachetés*. Gone is the custom of referring only to one's own journal — even though each journal still quietly reserves the right to refer to itself as "the Journal" in its own editorial columns; gone is the practice of debating matters of priority "en séance publique." Today, these controversial issues are resolved by cold documentation, and the ease of communication is such that the preliminary note may find its way into print within a few weeks if indeed it was not released to the Sunday supplement shortly after the idea was born.

RECLASSIFICATION OF PHYSICIANS IN PRIORITIES I AND II

Because of the imminent selection of Priority III physicians to fill current induction calls, according to a December 19 circular from Massachusetts State Headquarters for Selective Service, the Director of Selective Service, under the provision of Section 1625.3 of the regulations, has requested the immediate reopening of the classification of each Priority I and Priority II physician who is now deferred in Class II-A or III-A.

Under this newly ordered scrutiny occupational deferments will be continued only when it can be demonstrated that the medical services of the special registrant are absolutely essential to the medical needs of the community; those who are considered thus essential will thereupon be classified in Class II-A, the others in Class I-A, subject to immediate call for duty.

It may be of some comfort for special registrants to know, the Director of Selective Service believes, that they are generally commissioned in the grades of first lieutenant, captain or above, the first two grades of which, if there are dependents but no prior military service, are eligible to receive gross monthly incomes of approximately $501 and $576 respectively.

Military duty under certain prescribed conditions is, at the moment, the law of the land, and its requirements fall hardest on the medical profession, which is, in effect, the victim of obviously discriminatory legislation. Where inequities appear to exist an effort should be made to correct them in the new law that must be passed by the next Congress.

Dr. Wm. Wood gives an account in the London Lancet (see this Journal, March 19th, 1851), of a man confined in the Bethlehem Hospital on account of insanity, who became completely restored to his health and reason, after a tapeworm had been discharged by the administration of kousso.

Boston M. & S. J. *January 12, 1853*

CORRESPONDENCE

ECHO OF THE PAST

To the Editor: Back in 1940 the graduates of Middlesex University School of Medicine raised a fund for the purpose of reorganizing and improving their Alma Mater, and to obtain official recognition of the school. Some of the money so raised was spent in what proved to be fruitless efforts for this purpose. Litigation instituted on behalf of the school to compel its approval by the state authorities was unsuccessful, and the school itself ultimately closed its doors. There was left in the hands of the association organized for the foregoing purposes a large sum of money, which is to be returned, as far as possible, to the contributors. To accomplish this purpose a petition has been brought to the court for instructions regarding its disposition, and William J. O'Neill, of 40 Court Street, Boston, and John C. Johnston, of 22 Chestnut Street, Boston, have been appointed co-receivers. They have been ordered to give notice to all persons in interest to file claims with either of them on or before the fifteenth day of January, 1953, or be forever barred. This order of notice has been published, as ordered by the court, in the *Boston Traveler*. Knowing, however, that it may not come to the attention of the parties in interest, the receivers have thought it best to insert an advertisement in this journal and have requested the editors to give the matter some publicity in the form of the present communication. It is hoped that as many as possible will co-operate by sending to either of the receivers at his above address proofs of claim. These proofs of claim should be sworn to, and if possible checks, receipts or other evidence of the contribution should be annexed thereto.

J. C. Johnston

Boston

NONCLINICAL NOTES

APPOINTMENT OF DR. BABCOCK

Dr. Henry H. Babcock was recently appointed superintendent and physician-in-chief of Butler Hospital, Providence, Rhode Island, succeeding Dr. Arthur H. Ruggles. Dr. Babcock had previously served as acting superintendent and physician-in-chief since May 10, 1951. He joined the staff of Butler Hospital in May, 1946, and was director of the Out-Patient Department from 1949 to 1951.

GEORGE M. SMITH BOOK FUND

The George M. Smith Book Fund has been established at Yale University School of Medicine in honor of the late Dr. George Milton Smith. The income of this fund will be used to purchase books on subjects of occupational medicine and hygiene, to be placed in the Yale Medical Library with an appropriate bookplate. The present collection of books on this subject is small, and reference volumes on industrial medicine, nursing, engineering and chemistry are constantly in demand. Continuing pressure for intelligent use of employed manpower makes it imperative that the School of Medicine have the best information available for all concerned with this growing field of endeavor. These books will of course be freely available to physicians and to hospitals throughout Connecticut, in accordance with the Library's regular policies.

Contributions may be sent to Dr. J. Wister Meigs, 333 Cedar Street, New Haven, made payable to Yale University for the George M. Smith Book Fund. Such gifts are deductible for tax purposes.

HONORARY DEGREE FOR DR. COBB

Dr. Stanley Cobb, professor of neuropathology at Harvard Medical School and psychiatrist-in-chief at the Massachusetts General Hospital, received an honorary degree of Doctor of Science from the University of Maryland at the opening of the new Psychiatric Institute in Baltimore on Monday, November 17.

NOTICES

COMBINED MEETING OF GREATER BOSTON MEDICAL AND DENTAL SOCIETIES

A combined meeting of the Greater Boston Medical and Dental Societies will be held at the Shelton Hotel on January 21. Dinner will be served at 6:30 p.m. At 8 p.m., David Weisberger, M.D., D.M.D., professor of oral medicine, Harvard School of Dental Medicine, and oral surgeon and chief of Dental Service, Massachusetts General Hospital, will speak on the subject "The Tongue as a Diagnostic Index."

SOCIETY MEETINGS AND CONFERENCES

JANUARY 9. Massachusetts Society of Anesthesiologists. Page 1050, issue of December 25.

JANUARY 9–30. Combined Anesthesia Teaching Conferences of Boston. Page 785, issue of November 13.

JANUARY 10–31. Springfield Hospital Educational Program. Page 1000, issue of December 18.

JANUARY 12–MARCH 23. Postgraduate Course in General Medicine. Cushing Veterans Administration Hospital, Framingham. Page 697, issue of October 30.

JANUARY 13. Springfield Academy of Medicine. Page 1001, issue of December 18.

JANUARY 13. Harvard Medical Society. Page 41, issue of January 1.

JANUARY 14. Essex North District Medical Society. Page 743, issue of November 6.

JANUARY 14–28. Lahey Clinic Lectures. Page 1050, issue of December 25.

JANUARY 14–APRIL 8. Postgraduate Medical Institute. Boston. Page 452, issue of September 18.

JANUARY 19–APRIL 20. Hartford Medical Society. Page 42, issue of January 1.

JANUARY 20. South End Medical Club. Page 41, issue of January 1.

JANUARY 21. Combined Meeting of Greater Boston Medical and Dental Societies. Notice above.

JANUARY 21. Boston Graduate Club of Phi Delta Epsilon Medical Fraternity. Page 1050, issue of December 25.

JANUARY 21. New England Society of Physical Medicine. Page 41, issue of January 1.

JANUARY 28–APRIL 1. Postgraduate Medical Institute Course in General Medicine. Burbank Hospital, Fitchburg. Page 1049, issue of December 25.

JANUARY 30. First Public Health Workshop on Dental Care in Industry. Page 41, issue of January 1.

FEBRUARY 6. New England Society of Anesthesiologists. Page 827, issue of November 20.

FEBRUARY 6. American College of Radiology. Page 1001, issue of December 18.

FEBRUARY 7–JUNE 2. Mount Auburn Hospital Panel Discussions. Page 868, issue of November 27.

FEBRUARY 9 AND 10. Annual Congress on Medical Education and Licensure. Page 786, issue of November 13.

FEBRUARY 23 AND 24. American College of Surgeons. Page 42, issue of January 1.

MARCH 2–5. New Orleans Graduate Medical Assembly. Page 828, issue of November 20.

MARCH 2–MAY 4. Massachusetts Department of Mental Health. Postgraduate Seminar in Neurology and Psychiatry. Page 540, issue of October 2.

APRIL 3. New England Society of Anesthesiologists. Page 418, issue of September 11.

APRIL 29 AND OCTOBER 28. New England Obstetrical and Gynecological Society. Page 868, issue of November 27.

MAY 25–31. First World Congress on Fertility and Sterility. Page 1001, issue of December 18.

DISTRICT MEDICAL SOCIETIES

ESSEX NORTH

JANUARY 14. Pentucket Club, 111 Main Street, Haverhill.

MAY 13. Andover Country Club, Shawsheen.

MIDDLESEX WEST

JANUARY 12–MARCH 23. Postgraduate Course in General Medicine. Cushing Veterans Administration Hospital, Framingham.

NORFOLK

JANUARY 27.

FEBRUARY 24.

MARCH 24.

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, JANUARY 15

THURSDAY, JANUARY 15

*8:30–10:00 a.m. Orthopedic Staff Conference. Boston City Hospital.
*9:00–10:00 a.m. Arthritis Grand Rounds. Robert Breck Brigham Hospital.
*11:00 a.m.–12:30 p.m. Hand Clinic (Physical Medicine and Rehabilitation Service). Boston City Hospital.
12:00 m. Consultation Rounds. Psychiatry. Cardiovascular. Boston City Hospital.
*5:00–6:00 p.m. Surgical Division Meeting. Mount Auburn Hospital, Cambridge.
*7:30 p.m. Interpretation of Electrocardiograms. Lectures and Demonstration given by Drs. E. E. Hinton, C. C. Bailey and Walter Goodale. New England Deaconess Hospital.
8:30 p.m. Staff meeting of the Bellevue Hospital. Contagious Diseases of Children. Dr. Louis Weinstein. Hotel Beaconsfield, Brookline.

FRIDAY, JANUARY 16

*10:00 a.m. Tuberculosis Surgical Clinic. South End Health Unit. 57 East Concord Street.
*10:00 a.m.–1:00 p.m. Medical and Surgical Grand Rounds. Dr. George W. Thorn and Dr. Francis D. Moore. Main Amphitheater, Peter Bent Brigham Hospital.
10:30–11:15 a.m. Diabetes Lecture. Dr. Elliott Joslin. New England Deaconess Hospital.
11:00 a.m.–12:00 m. Pediatric Conference. Mount Auburn Hospital, Cambridge.
12:00 m. Clinical Conference. Patient Presentation. Dowling Amphitheater, Boston City Hospital.
*1:30 p.m. Fertility and Endocrine Clinic. Free Hospital for Women, Brookline.
*4:00–10:00 p.m. Alcoholism Clinic. By appointment. Washingtonian Hospital, 41 Waltham Street.
*7:00–9:00 p.m. Combined Anesthesia Teaching Conferences of Boston. Problems of Anesthesia for Patients with Pulmonary Disease: Pulmonary Function Studies. Dr. Etsten. Amphitheater, Evans Memorial, Massachusetts Memorial Hospitals. Eighth Floor, 65 East Newton Street.
7:30 p.m. Massachusetts Society of Anesthesiologists. Joslin Amphitheater, New England Deaconess Hospital.
8:00 p.m. Boston Orthopedic Club. Meeting held jointly with New England Roentgen Ray Society. Bone Tumors. Dr. Isadore Snapper. Boston Medical Library, 8 Fenway.

SATURDAY, JANUARY 17

*9:00 a.m. Proctology Clinic. Peter Bent Brigham Hospital.
*9:00 a.m. Alcoholism Clinic. Peter Bent Brigham Hospital.
*11:00 a.m.–12:00 m. Blood Clinic. Dr. William Dameshek. Stearns Auditorium, New England Center Hospital.
12:00 m. Consultation Rounds. Pathology Rounds. Mallory Amphitheater. Boston City Hospital.

MONDAY, JANUARY 19

*8:00–9:00 a.m. Combined Medical and Surgical Rounds for Diabetic Surgery Cases. New England Deaconess Hospital.
*8:30–9:30 a.m. Clinic by entire Surgical Staff and Anesthesia Staff. Cheever Amphitheater, Dowling Building, Boston City Hospital.
12:00 m. Pediatric Medical-Surgical Conference (Boston Floating Hospital). Pratt Lecture Hall. Joseph H. Pratt Diagnostic Hospital.
*12:15–1:15 p.m. Clinicopathological Conference. Main Amphitheater, Peter Bent Brigham Hospital.
*7:00–9:00 p.m. Anesthesia Teaching Conference. Stearns Auditorium, New England Center Hospital.

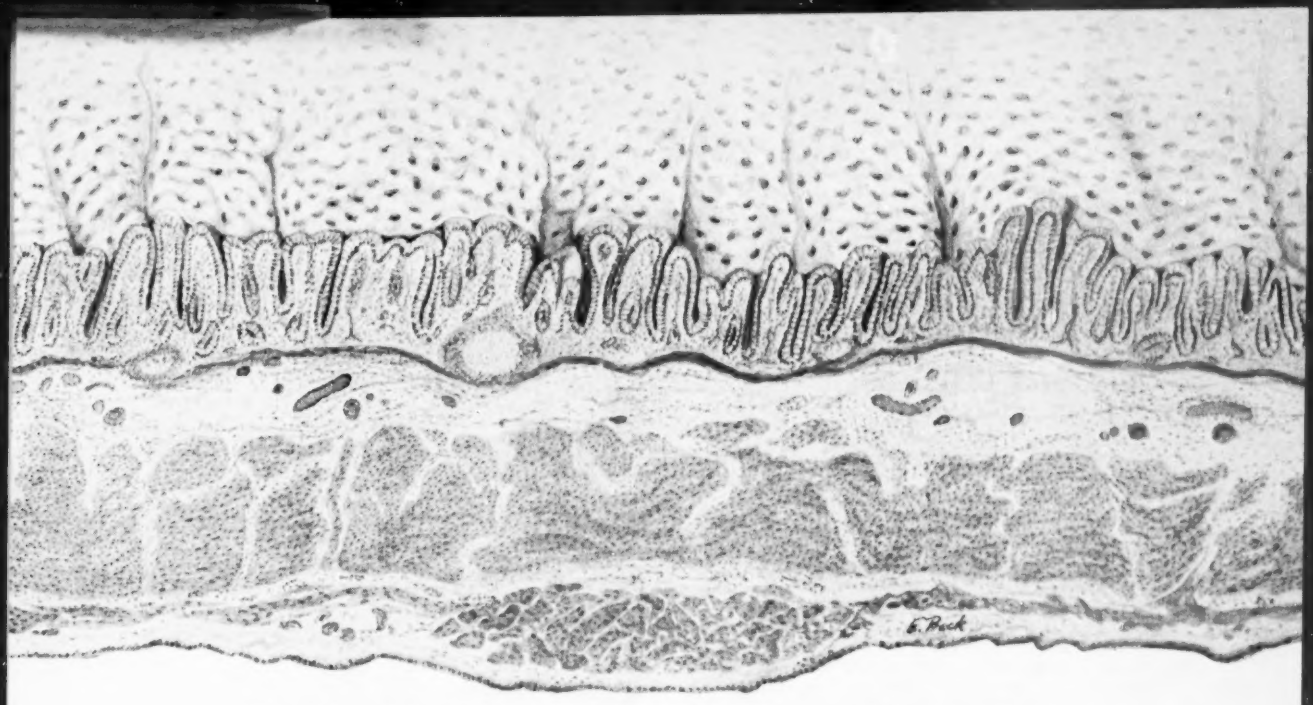
TUESDAY, JANUARY 20

*9:00 a.m. Geriatrics Clinic. Peter Bent Brigham Hospital.
12:00 m. Consultation Rounds. Gastrointestinal. Infectious Diseases. Boston City Hospital.
12:00 m. South End Medical Club. Headquarters of the Boston Tuberculosis Association, 554 Columbus Avenue.
*12:00 m.–1:00 p.m. Pediatric Rounds. Burnham Memorial Hospital for Children, Massachusetts General Hospital.
*12:15–1:15 p.m. X-ray Conference. Dr. Merrill Sosman. Main Amphitheater, Peter Bent Brigham Hospital.
*5:00–6:00 p.m. Service Meeting followed by Clinical Conference (Medical, Surgical, Obstetrical). Faulkner Hospital.

WEDNESDAY, JANUARY 21

*12:00 m. Boston State Hospital Psychiatric Seminar. Reception Building Auditorium, 591 Morton Street, Dorchester.
*12:00 m.–1:00 p.m. Clinicopathological Conference. (Children's Medical Center.) Jimmy Fund Building, 25 Binney Street.
12:30 p.m. Weekly Pathological Meeting. Joslin Amphitheater, New England Deaconess Hospital.
*4:00 p.m. Thoracic Conference. Held by Overholt Clinic. Harris Hall, New England Deaconess Hospital.
*4:00–5:30 p.m. Fracture Lecture. Boston City Hospital.
6:30 p.m. Combined Meeting (and Dinner) of the Greater Boston Medical and Dental Societies. Shelton Hotel.
*7:30 p.m. Lahey Clinic Lectures. Symposium on Radioactive Isotopes. Drs. Shields Warren, Elmer C. Bartels and John W. Norcross. Joslin Auditorium, New England Deaconess Hospital.
*8:00 p.m. New England Society of Physical Medicine. Massachusetts General Hospital.

*Open to the medical profession.



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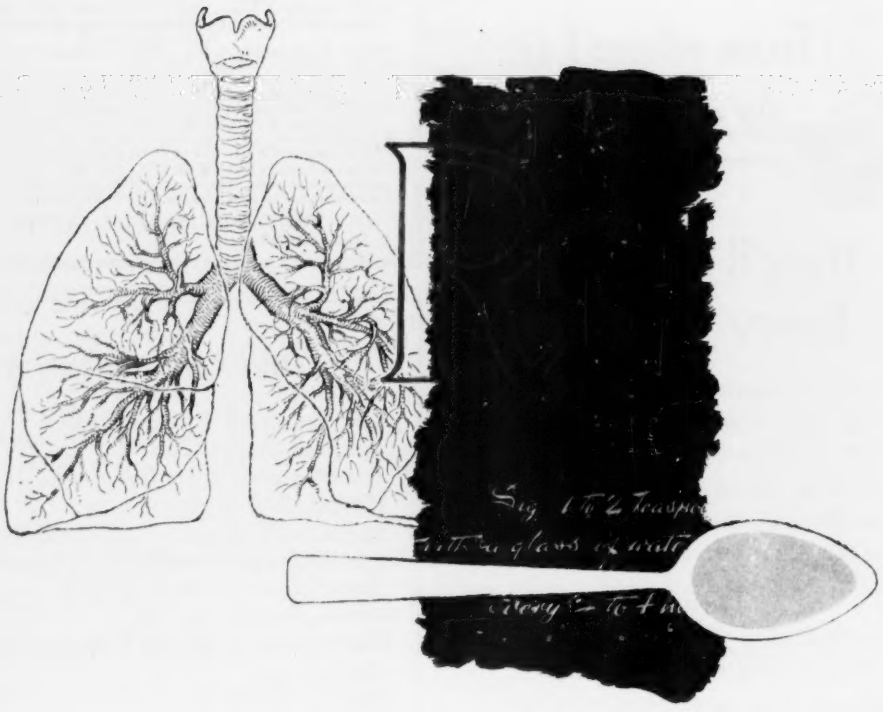

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